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C-17 SPIROLACTONIZATION AND 6,7 OXIDATION OF STEROIDS

Abstract:

Novel processes for the C-17 spirolactonization and 6,7 oxidation of steroid compounds are provided. In certain preferred embodiments, the present invention provides for the preparation of steroid compounds which are useful in the preparation of methyl hydrogen 9,11alpha-epoxy-17alpha-hydroxy-3-oxopregn-4-ene-7alpha, 21-dicarboxylate, -lactone (otherwise referred to as eplerenone or epoxymexrenone).

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WO 03/082895 A2

(54) Title: PROCESS TO PREPARE EPLERENONE

(57) Abstract: The present invention involves novel intermediates, including a 7α-substituted steriod (II), and various novel processes which are used to prepare known intermediates useful in the production of eplerenone, a pharmaceutical agent.

PROCESSES TO PREPARE EPLERENONE

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention includes a process for the transformation of a 3-enol ether $\Delta^{3,5}$-steroid to the corresponding $\Delta^{4,6}$-3-ketal steroid (I-P).

The present invention includes a process for the transformation of a $\Delta^{4,6}$-3-keto steroid or ketal thereof (I), to the corresponding Δ^{4}-3-ketosteroid-7α-carboxylic acid (VI).

The present invention also includes a novel processes and novel intermediates to produce the pharmaceutically useful compound eplerenone.

Further, the invention includes processes for transformation of 11α-hydroxy-17-lactone (CI) or 11α-hydroxy steroids (CIV) to the corresponding $\Delta^{9(11)}$-17-lactone (CII) or $\Delta^{9(11)}$-steroids (CV) using a N-fluoroalkylamine reagents (CVI).

2. Description of the Related Art

It is known to transform 3-keto-$\Delta^{4,6}$-steroids into the corresponding steroidal $\Delta^{4,6}$-3-ketals by acid-catalyzed ketalization. Yields are moderate and double bond deconjugation can be competitive. For example, $\Delta^{4,6}$-cholestadiene-3-one-3-cycloethyleneketal was prepared by ketalization of $\Delta^{4,6}$-cholestadien-3-one in 64% yield, see *J. Org. Chem.* 26, 2549 (1961). Also, 17β-hydroxyandrosta-4,6-dien-3-one-3-cycloethyleneketal was prepared by ketalization of 6-dehydrotestosterone in 55% crude yield, see *J. Am. Chem. Soc.*, 86, 2183 (1964). The steroidal $\Delta^{4,6}$-3-ketals (I-P) can be used as starting materials in the process to prepare eplerenone.

J. Org. Chem., 29, 601 (1964) reports that $\Delta^{3,5}$-3-alkoxy steroids react with DDQ in the presence of water to give the corresponding $\Delta^{4,6}$-3-keto steroids. The process of the present invention reacts $\Delta^{3,5}$-3-alkoxy steroids (3-alkyl enol ether) with DDQ in the presence of an alcohol under essentially anhydrous conditions to give the $\Delta^{4,6}$-3-ketal steroid (I-P). In addition, the prior art methods of producing the $\Delta^{4,6}$-3-ketal steroid (I-P) uses two steps, 6-dehydrogenation of an enol ether to a $\Delta^{4,6}$-3-keto steroid followed by ketalization whereas the present invention is a one step reaction.

Eplerenone, also known as epoxymexrenone, is a useful pharmaceutical agent and chemically is 9α,11α-epoxy-17β-hydroxypregn-4-en-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester.

International Publication WO98/25948 of PCT application PCT/US97/23090 discloses eplerenone and many different process to prepare eplerenone. In particular, see schemes 1 thru 10.

US Patent 4,874,754 discloses 19-nor steroids with 7α-aryl substitution. The 7α-aryl substituent included a number of groups including phenyl, thienyl, furyl, thiazolyl, pyrrolyl, oxazolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, isothiazolyl and isoxazolyl, pyridinyl, pyridazinyl, pyrimidinyl and pyrazinyl. Regardless of which group was used, the 19-nor compounds had antiproliferative, anti-estrogenic and/or estrogenic properties and are not useful intermediates to eplerenone because there are no practical methods for installing the 19-methyl group into 19-nor steroids. The 7α-substituted steroids (II) of the present invention, are intermediates, not end products and do not have estrogenic properties because they are not 19-nor steroids.

US Patent 4,502,989 discloses a number of Δ^{11}-steroidal-γ-lactones many of which are substituted in the 7α-position which have aldosterone antagonist activity. The 7α-substitution is 6α,7α-methylene-, 7α-trimethylacetylthio-, 7α-acetylthio- and 7α-benzoythio-, see claim 1. These compounds differ from the compounds of the invention in that the C-ring double bond is Δ^{11}- and the 7α-substitutents are such that the compounds cannot be used in the same way as the 7α-substituted steroids (II).

Het., 25, 399 (1987) and *Bull. Soc. Chim. Fr.* 131, 900 (1994) disclose the use of boron trifluoride diethyl etherate to catalyze conjugate addition of non-steroidal 2-methylfuran to α,β-unsaturated ketones in ethanol/nitromethane. The process of the present invention involves steroidal furans. In addition, the enone substrates in *Het.*, 25, 399 (1987) and *Bull. Soc. Chim. Fr.* 131, 900 (1994) do not contain stereocenters, so the issue of stereocontrol does not arise.

Methods for conjugate addition of carbon nucleophiles to 9(11)-saturated-$\Delta^{4,6}$-3-keto steroids to give 9(11)-saturated-7α-substituted steroids stereoselectively are known. *J. Am. Chem. Soc.*, 94, 4654 (1972) discloses conjugate addition of carbon nucleophiles to 9(11)-saturated-$\Delta^{4,6}$-3-keto steroids to give 9(11)-saturated-7α-substituted steroids stereoselectively. *Tet.*, 49, 9955 (1993) and *Tet. Lett.*, 29, 1533 (1988) disclose stereoselective addition of allyltrimethylsilane to canrenone (titanium tetrachloride, methylene chloride, -78°) to give a mixture of two difficult-to-separate products (7α-allyl-canrenone and the corresponding 6α,7α-fused silylcyclopentane) in

poor yields (43-73% and 7-15%, respectively). Note that in these cases the steroid substrate is 9(11) saturated. All attempts to apply these methods or similar methods to 9(11) unsaturated steroid substrates have failed, due to lack of stereocontrol. For example, US Patent 4,559,332, Example 7, discloses that trimethylsulfoxonium iodide adds to $\Delta^{9(11)}$-canrenone (I) using sodium hydride in DMSO at room temperature to give exclusively 6β,7β-methylene-$\Delta^{9(11)}$-canrenone. Also, nitromethane adds to $\Delta^{9(11)}$-canrenone (I) in tetramethylguanidine at room temperature over 7.5 hrs.) to give exclusively the 7β stereoisomer (7β-nitromethyl-$\Delta^{9(11)}$-6,7-dihydrocanrenone.

Helv. Chim. Acta, 80, 566 (1997) and US Patent 4,559,332 disclose that reaction of $\Delta^{9(11)}$-canrenone with diethylaluminum cyanide to give 7α-cyano-$\Delta^{9(11)}$-6,7-dihydrocanrenone, but the crude product is described as a "brownish amorphous residue" that "was filtered through silica gel yielding amorphous" semipurified product "which was used without further purification in the next step." The ratio of 7-α to 7-β epimers is not disclosed.

J. Am. Chem. Soc. 79, 3120 (1957), *J. Am. Chem. Soc. 82*, 6136 (1960), and *J. Org. Chem. 27*, 1192 (1962) disclose degradation of non-steroidal enediones to carboxylic acids through alkoxyhydroperoxide intermediates and not hydroxyhydroperoxide intermediates. The process of the present invention involves steroidal enediones.

The oxidative opening of furans to carboxylic acids, or carboxylic acid derivatives, by direct ozonolysis is known. However, the yields are usually quite poor. *J. Org. Chem.*, 61, 9126 (1996), reported that a 2,5-disubstituted furan on ozonization underwent partial cleavage to an enol acetate rather than complete cleavage to the carboxylic acid. *Het.*, 34, 895 (1992) reported direct ozonization of a 2-substituted furan gave, after esterification, the methyl ester in 59% yield. *J. Am. Chem. Soc.* 101, 259 (1979) reported direct ozonization of a 2-substituted furan gave, after esterification, the methyl ester in 55% yield. *J. Am. Chem. Soc.*, 107, 7762 (1985) reported direct ozonization of a 2-sugar-substituted furan gave, after borane reduction, the primary alcohol in 50% yield. *Tet. Lett.*, 34, 7323 (1993) reported direct ozonization of a 2-substituted furan gave, after esterification, the methyl ester in 60% yield. *Carb. Res.*, 150, 163 (1986) reported direct ozonization of a 2-sugar-substituted furan afforded, after reduction with triphenylphosphine followed by

lithium aluminum hydride, the primary alcohol in 11% yield. *Tet. Lett.*, 22, 141 (1981) reported direct ozonization of a 2-substituted furan gave, after oxidative workup, the carboxylic acid in approximately 30% yield. *J. Am. Chem. Soc.*, 109, 2082 (1987) reported direct ozonization of a 2-substituted furan gave, after esterification, the methyl ester in 77% yield. *Tet. Lett.*, 39, 7013 (1998) reported direct ozonization of a 2-substituted furan gave, after esterification, the methyl ester in 78%-87% yield. *J. Org. Chem.*, 54, 2085 (1989) reported direct ozonization of two 2-substituted furans gives the carboxylic acid in 89-95% yield, however, in this study, the 2-substituted furans were very simple (i.e., they did not contain any reactive functional group other than the furan). There is no disclosures of a two step furan opening and then oxidative cleavage to the carboxylic acid which results in high yields.

J. Org. Chem. 63, 7505 (1998) discloses the use of dibromatin, sodium bicarbonate and aqueous acetone to open non-steroidal furans to produce enediones. The process of the present invention involves steroidal furans.

Chem. Lett., 1771 (1983) discloses the use of hydrochloric acid in ether to catalyze the isomerization of non-steroidal *cis*-enediones to *trans*-enediones. The process of the present invention involves steroidal enediones.

J. Am. Chem. Soc., 79, 3120 (1957), *J. Am. Chem. Soc., 82*, 6136 (1960) and *J. Org. Chem.*, 27, 1192 (1962) disclose the degradation of enediones to carboxylic acids through alkoxyhydroperoxide intermediates by use of ozone and an oxidatively cleaving agent. The yields are not particularly high. For example, the yield of benzoic acid from *trans*-dibenzoylethylene was 54%. Following this process, methoxyhydroperoxide (IV-OOH) (where R_{7-2} = $-CH_3$) gave a 65.2/34.8 mixture of the desired carboxylic acid (VI) and α-ketomethylester where (R_b = OMe). The α-ketomethyl ester can not be transformed to an eplerenone useful compound and its production makes this process not commercially useful. By contrast, in the process of this invention, the enedione (III) is degraded to the carboxylic acid (VI) through the hydroxyhydroperoxide intermediate (IV-OOH, where R_{7-2} = -H), which surprisingly rearranges to the desired carboxylic acid (VI) in nearly quantitative yield. The process of the present invention uses ozone, a hydroperoxy-deoxygenating agent and then a

oxidatively cleaving agent to avoid production of the α-ketomethylester and obtain increased yields.

Drugs of the Future, 24, 488 (1999) discloses conversion of the 5,7-lactone (VII) to the corresponding methyl ester (VIII) by treatment with "methyl iodide in basic medium,". The process of the present invention for methylation is a sequential process.

International Publication WO98/25948 generically discloses (5,7)-17-bislactones and 3 protected forms.

International Publication WO98/25948 discloses the transformation of a steroidal 7α-acid to the (5,7)-17-bislactone. This process requires an orthoester. The process of the present invention does not require an orthoester.

International Publication WO98/25948 discloses the transformation of a (5,7)-17-bislactone to the corresponding 7α-CO-OCH_3 in one step. The present invention uses two steps but obtains better yields and consumes less reagent.

Eplerenone is 9(11)α-epoxy-17β-hydroxypregn-4-en-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester and as such contains a 7α-carbomethoxy substituent. From the standpoint of production, a major difficulty in the production of eplerenone is introduction of the 7α-carbomethoxy substituent. The present invention includes an improved proved process for the introduction of the 7α-substitutent.

It is known that a carboxylic acid can be obtained from a (substituted)furan in one step by ozonolysis. However, the yields are quite low. Further, it is known that furans can be opened to enediones. It is also known that enediones can be oxidized to carboxylic acids.

Bulletin of the Chemical Society of Japan, 52, 3377-3380 (1979) discloses that N-(1,1,2,2,3,3,3)hexafluoropropyldiethylamine, "Ishikawa reagent" is used to replace a hydroxyl group with a fluorine atom or eliminate a hydroxyl group to an olefin. With cyclohexanol, a simple monocyclic system, the elimination product olefin was 78%. However, when the "Ishikawa reagent" was applied to a steroid, cholesterol, the corresponding fluoro compound cholesteryl fluoride was obtained in 83% yield; no elimination product was reported.

J. Org. Chem., 2187-2195(1964) discloses the reaction of 11α-hydroxypregn-4-ene-3,20-dione with 2-chloro-1,1,2-trifluorotriethylamine to give the elimination

product, pregna-4,9(11)-diene-3,20-dione, in 86% yield. The process of the present invention does not use 2-chloro-1,1,2-trifluorotriethylamine also known as Yarovenko reagent. Further, use of 2-chloro-1,1,2-trifluorotriethylamine is a problem because it is not stable enough to make scale up practicable. In addition, it is derived from a chlorofluorocarbon and is not environmentally sound.

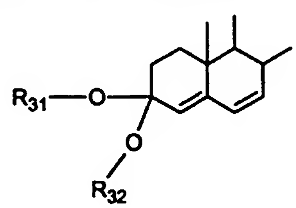
Tetrahedron Letters, 1065-1069 (1962) also discloses the reaction of 11α-hydroxypregn-4-ene-3,20-dione with 2-chloro-1,1,2-trifluorotriethylamine to give the elimination product, pregna-4,9(11)-diene-3,20-dione.

Steroids, 29, 2187 (1964) discloses the reaction of steroidal alcohols with 2-chloro-1,1,2-trifluorotriethylamine to replace the hydroxyl group with fluorine. The present invention does not use 2-chloro-1,1,2-trifluorotriethylamine, nor does it replace a hydroxyl group with a fluorine atom.

J. Fluorine Chem., 109, 25-31 (2001) describes and compares the use of 1,1,2,2-tetrafluoroethyl-N,N-dimethylamine as well as Yarovenko-Raksha and Ishikawa reagent as fluorinating and dehydrating agents. While the document discloses examples of elimination reactions in both aliphatic and cyclic systems, the primary use is as a fluorinating agent. The only steroid example was the reaction of 1,1,2,2-tetrafluoroethyl-N,N-dimethylamine with cholesterol which produced a product with fluorine at the C-3 position of cholesterol.

SUMMARY OF INVENTION

Disclosed is a process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P)



(I-P)

where R_{31} and R_{32} are

(1) the same or different and are C_1-C_3 alkyl, and

(2) taken with the attached -O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

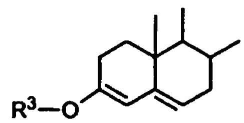
where R_{33} and R_{34} are the same or different and are

-H,

C_1-C_3 alkyl,

which comprises

(1) contacting a $\Delta^{3,5}$-3-enol ether of formula (Alkyl enol ether)



(Alkyl enol ether)

where R^3 is

C_1-C_3 alkyl,

CH_3-CO-,

Φ-CO- or

$R_{Si-1}R_{Si-2}R_{Si-3}Si$- where R_{Si-1}, R_{Si-2} and R_{Si-3} are the same or different and are C_1-C_4 alkyl; with a hydride abstractor and an alcohol selected from the group consisting of alcohols of the formula:

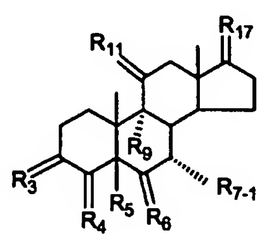
(a) R_{31}-OH, where R_{31} is as defined above,

(b) R_{32}-OH, where R_{32} is as defined above,

(c) HO-(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)-OH where n_1, R_{33} and R_{34} are as defined above,

(d) HO-CH_2-CH_2-OH.

Also disclosed is a 7α-substituted steroid of formula (II)



(II)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(II) R_3 is R_{3-3}:R_{3-4} and R_4 is R_{4-3}:R_{4-4} where one of R_{3-3} and R_{3-4} is –O-R_{31} where R_{31} is C_1-C_3 alkyl, the other of R_{3-3} and R_{3-4} is taken together with one of R_{4-3} and R_{4-4} to form a second bond between the carbon atoms to which they are attached,

and the other of R_{4-3} and R_{4-4} is –H; R_6 is R_{6-3}:R_{6-4} where one of R_{6-3} and R_{6-4} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-3} and R_{6-4} is –H; (III)

R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

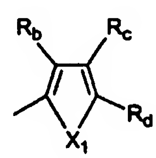
$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

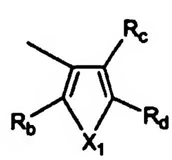
(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_{7-1} is a molecular fragment of the formula (-A1)



(-A1)

or of the formula (-A2)



(-A2)

where X_1 is:

–S-,

-O- or

–NX_{1-1}- and where X_{1-1} is:

-H,

C_1-C_4 alkyl,

-CO-OX_{1-2} where X_{1-2} is C_1-C_4 alkyl or –CH_2-φ,

-CO-X_{1-2} where X_{1-2} is as defined above,

-CO-φ where –φ is substituted in the *o*-position with –CO-O-(C_1-C_4 alkyl),

-SO_2-(C_1-C_3 alkyl),

-SO_2-φ where φ is optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

–CO-OCH_3 and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl;

C_1-C_4 alkoxy;

-CH_2-OR_{d-1} where R_{d-1} is –H or C_1-C_4 alkyl,

-CH_2-N(R_{d-6})$_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R_{d-6a} where R_{d-6a} is C_1-C_4 alkyl or –φ,

-CH_2-O-CO-R_{d-1} where R_{d-1} is as defined above,

-CH(OR_{d-1})$_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

-CH_2-CH_2-,

-CH_2-CH_2-CH_2-,

-CH_2-C(CH_3-)$_2$-CH_2-,

-CH(-O-CO-R_{d-1})$_2$ where R_{d-1} is as defined above,

-Si(R)$_3$ where R is as defined above,

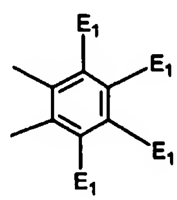
-O-Si(R)$_3$ where R is as defined above,

-Sn(R_{b-1})$_3$ where R_{b-1} is as defined above,

-S-R_{d-5} where R_{d-5} is C_1-C_4 alkyl or –φ,

-N(R_{d-6})$_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

-OE_{1-1} where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

–$SiE_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

-S-E_{1-5} where E_{1-5} is C_1-C_4 alkyl or –φ,

-S-(O)$_{1-2}$-E_{1-5} where E_{1-5} is as defined above,

-$N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are as defined above,

-$P(O)(O-E_{1-1})_2$ where E_{1-1} is as defined above,

-$Si(R)_3$ where R is as defined above;

-CE_1=M (-B)

where E_1 is as defined above and

where M is:

(1) =O,

(2) =N-E_2 where E_2 is selected from the group consisting of

-H

C_1-C_4 alkyl,

C_1-C_4 alkenyl containing 1 or 2 double bonds,

C_1-C_4 alkynyl containing 1 triple bond,

-CO-OE_{2-1} where E_{2-1} is –H or C_1-C_4 alkyl,

-$C(E_{2-1})_2$-OE_{2-2} where E_{2-1} are the same or different and are as defined above and where E_{2-2} is

C_1-C_4 alkyl,

-φ or

–$Si(R)_3$ where the three R are the same or different and are defined above,

-OE_{2-2} where E_{2-2} is as defined above,

-S-E_{2-3} where E_{2-3} is C_1-C_4 alkyl or –φ,

-S-$(O)_{1-2}$-E_{2-3} where E_{2-3} is as defined above,

-$N(R_{d-6})_2$ where the two R_{d6} are the same or different and are as defined above;

-$Si(R)_3$ where the three R are as defined above;

(3) =$C(E_2)_2$ where the E_2 are the same or different and are as defined above,

where E_1 and E_2 are taken together with the atoms to which they are attached to form a ring of 5 thru 7 members, optionally containing 3 thru 5

–O-,

-S-,

–N=,

-NX_{1-1}- where X_{1-1} is as defined above,

-CE_2= where E_2 is as defined above,

-$C(R_b)_2$- where R_b is as defined above, and optionally containing 1 or 2 additional double bonds;

$$-C{\equiv}C-E_2 \qquad (-C)$$

where E_2 is as defined above;

$$-CH_2-CH{=}CH_2 \qquad (-D1)$$

$$-CH{=}C{=}CH_2 \qquad (-D2)$$

$$-CH_2-C{\equiv}C-H \qquad (-D3)$$

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of

-$Si(-CH_3)_3$,

-$Si(-CH_2-CH_3)_3$,

-$CO-CH_3$,

-CO-H and

-$SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above, and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above, with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si(R_{17-1-2})$_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP), where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP), where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-$(CH_2)_{0-3}$-CH_3;

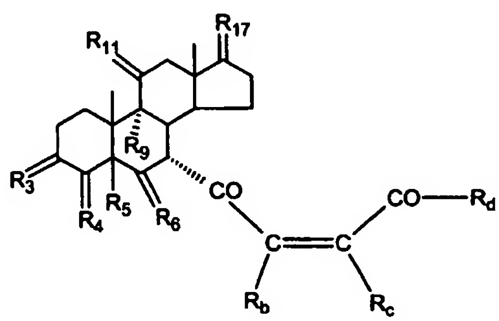
(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-CH_2······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

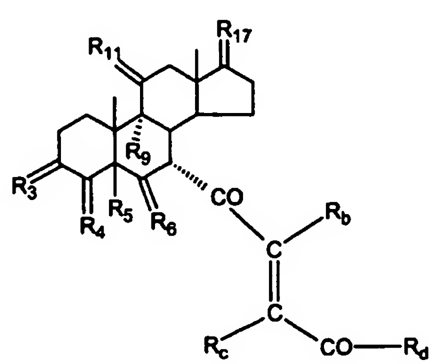
(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is –$(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH.

Further disclosed is a *cis* enedione of the formula (III-*cis*)



(III-cis)

and a trans enedione of the formula (III-*trans*)



(III-trans)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9, R_{11} R_{17} are as defined above;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

-CO-OCH$_3$ and

-CO-R$_{c-1}$ where R$_{c-1}$ is C$_1$-C$_4$ alkyl or –φ;

where R$_d$ is selected from the group consisting of

–H,

-C≡N,

C$_1$-C$_{10}$ alkyl;

C$_1$-C$_4$ alkoxy;

-CH$_2$-OR$_{d-1}$ where R$_{d-1}$ is –H or C$_1$-C$_4$ alkyl,

-CH$_2$-N(R$_{d-6}$)$_2$ where the two R$_{d-6}$ are the same or different and are:

C$_1$-C$_4$ alkyl,

-φ,

-CO-R$_{d-6a}$ where R$_{d-6a}$ is C$_1$-C$_4$ alkyl or –φ,

-CH$_2$-O-CO-R$_{d-1}$ where R$_{d-1}$ is as defined above,

-CH(OR$_{d-1}$)$_2$ where R$_{d-1}$ is as defined above and where the two R$_{d-1}$ taken together are:

-CH$_2$-CH$_2$-,

-CH$_2$-CH$_2$-CH$_2$-,

-CH$_2$-C(CH$_3$-)$_2$-CH$_2$-,

-CH(-O-CO-R$_{d-1}$)$_2$ where R$_{d-1}$ is as defined above,

-Si(R)$_3$ where R is as defined above,

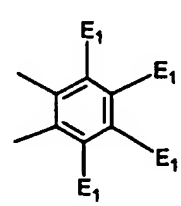
-O-Si(R)$_3$ where R is as defined above,

-Sn(R$_{b-1}$)$_3$ where R$_{b-1}$ is as defined above,

-S-R$_{d-5}$ where R$_{d-5}$ is C$_1$-C$_4$ alkyl or –φ,

-N(R$_{d-6}$)$_2$ where R$_{d-6}$ is as defined above,

where R$_c$ and R$_d$ taken together with the atoms to which they are attached to form



where E$_1$ are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

-OE_{1-1} where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

–$SiE_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

-S-E_{1-5} where E_{1-5} is C_1-C_4 alkyl or –φ,

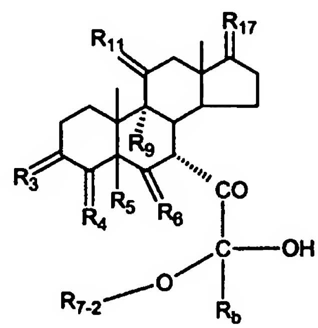
-S-$(O)_{1-2}$-E_{1-5} where E_{1-5} is as defined above,

-$N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are as defined above,

-$P(O)(O$-$E_{1-1})_2$ where E_{1-1} is as defined above,

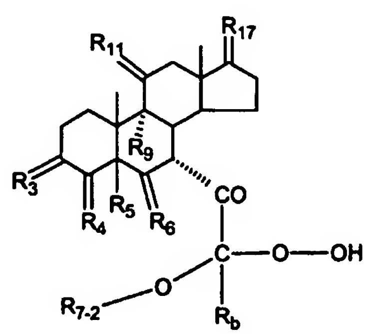
-$Si(R)_3$ where R is as defined above.

Further disclosed is a hydroxy compound of formula (IV-OH)



(IV-OH)

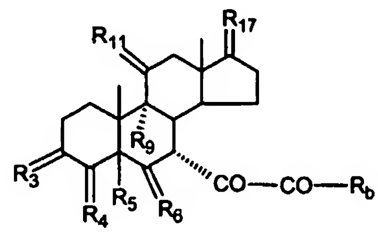
and a hydroperoxy compound (IV-O-OH)



(IV-OOH)

where R_3, R_4, R_5 and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_9, R_{11} R_{17} and R_b are as defined above and where R_{7-2} is –H and C_1-C_4 alkyl optionally substituted with one or two –OH.

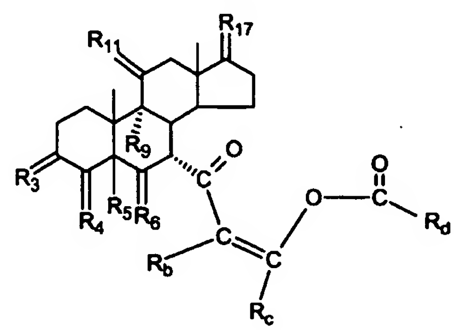
Disclosed is a biscarbonyl compound of the formula (V)



(V)

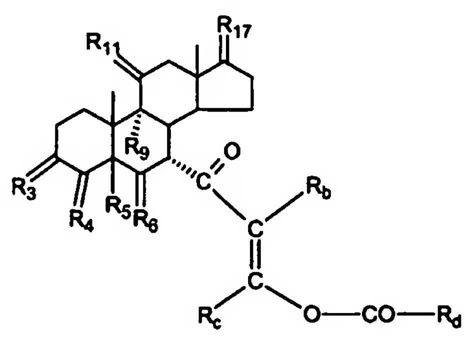
where R_3, R_4, R_5 and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_9, R_{11} R_{17} and R_b are as defined above.

Also disclosed is a cis oxyenedione of the formula (X-*cis*)



(X-cis)

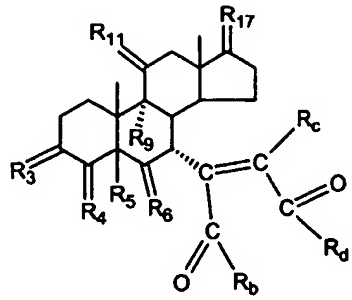
and a trans enedione of the formula (X-*trans*)



(X-trans)

where R_3, R_4, R_5 and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_9, R_{11} R_{17}, R_b, R_c and R_d are as defined above.

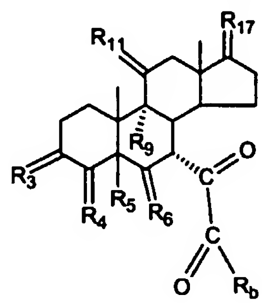
Further disclosed is a 7α-unsaturated steroid of formula (XIV)



(XIV)

where R_3, R_4, R_5 and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_9, R_{11} R_{17}, R_b and R_d are as defined above.

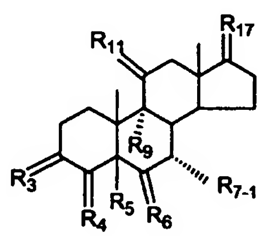
Additionally disclosed is a 7α-preacid of the formula (XV)



(XV)

where R_3, R_4, R_5 and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_9, R_{11} R_{17} and R_b are as defined above.

Disclosed is a process for the preparation of a 7α-substituted steroid (II) of the formula



(II)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(II) R_3 is R_{3-3}:R_{3-4} and R_4 is R_{4-3}:R_{4-4} where one of R_{3-3} and R_{3-4} is –O-R_{31} where R_{31} is C_1-C_3 alkyl, the other of R_{3-3} and R_{3-4} is taken together with one of R_{4-3}

and R_{4-4} to form a second bond between the carbon atoms to which they are attached, and the other of R_{4-3} and R_{4-4} is –H; R_6 is R_{6-3}:R_{6-4} where one of R_{6-3} and R_{6-4} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-3} and R_{6-4} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

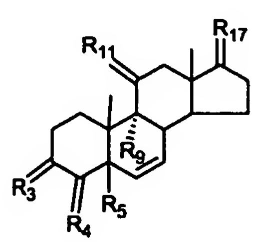
where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_{7-1}, R_9, R_{11} and R_{17}, are as defined above;

which comprises:

(1) contacting a $\Delta^{4,6}$-3-keto steroid or ketal thereof (I) of the formula



(I)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached;

(I-ketal) R_3 is R_{3-9}:R_{3-10} where R_{3-9} is $-O-R_{31}$ and R_{3-10} is $-O-R_{32}$ where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached $-O-C-O-$ to form a cyclic ketal of 5 or 6 atoms of the formula

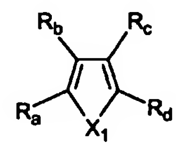
$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are $-H$ and C_1-C_3 alkyl; R_4 is R_{4-9}:R_{4-10} where one of R_{4-9} and R_{4-10} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-9} and R_{4-10} is $-H$;

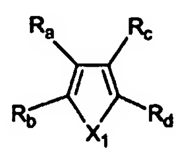
where R_9, R_{11} and R_{17} are as defined above, with an adduct selected from compounds

(a) of the formula (A)



(A1)

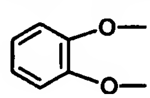
or



(A2)

where X_1, R_b, R_c and R_d are as defined above, and

where R_a is selected from the group consisting of $-H$, -ZnL, -BL, $-SiL_3$, $-SnL_3$, -Cu, -CuL, $-AlL_2$, -HgL, -Ag, -MgL, -Li and $-COOH$, where L is $-OH$, C_1-C_4 alkyl, -F, -Cl, -Br, -I, -CN, $-O(C_1$-C_3 alkyl), 2-thienyl, $(CH_3)_2C(O-)-C(O-)C(CH_3)_2$ and



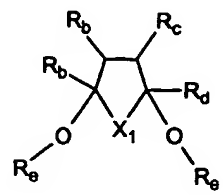
;

(b) of the formula (A')

$$R_b\text{-CO-CHR}_b\text{-CHR}_c\text{-CO-}R_d \qquad (A')$$

where R_b, R_c and R_d are as defined above;

(c) of the formula (A'')



(A")

where R_e is:

C_1-C_4 alkyl,

-CO-(C_1-C_4 alkyl or $-\varphi$),

$-Si(R)_3$ where R is as defined above and where X_1, R_b, R_c and R_d are as defined above;

(d) of the formula (B)

$$R_a\text{-}CE_1\text{=}M \qquad (B)$$

where R_a, E_1 and M are as defined above;

(e) of the formula (C)

$$R_a\text{-}C\equiv C\text{-}E_2 \qquad (C)$$

where R_a and E_2 are as defined above;

(f) of the formulas (D1, D2 and D3)

$$R_a\text{-}CH_2\text{-}CH\text{=}CH_2 \qquad (D1)$$

$$R_a\text{-}CH\text{=}C\text{=}CH_2 \qquad (D2)$$

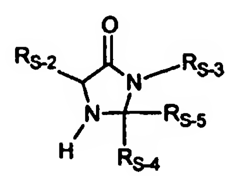
$$R_a\text{-}CH_2\text{-}C\equiv C\text{-}H \qquad (D3)$$

where R_a is as defined above, in the presence of:

(1) a Lewis Acid,

(2) a proton acid with a pK_a of < about 5 or

(3) a salt of a secondary amine of the formula



where:

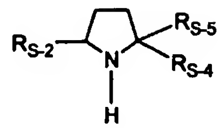
$R_{S\text{-}2}$ is –H, C_1-C_4 alkyl, $-\varphi$, and $-CH_2$-φ;

$R_{S\text{-}3}$ is –H, C_1-C_4 alkyl;

$R_{S\text{-}4}$ is –H, C_1-C_4 alkyl, $-\varphi$;

R_{S-5} is –H, C_1-C_4 alkyl, –φ;

and



where

R_{S-2} is –H, C_1-C_4 alkyl, –φ, and -CH_2-φ;

R_{S-4} is –H, C_1-C_4 alkyl, –φ;

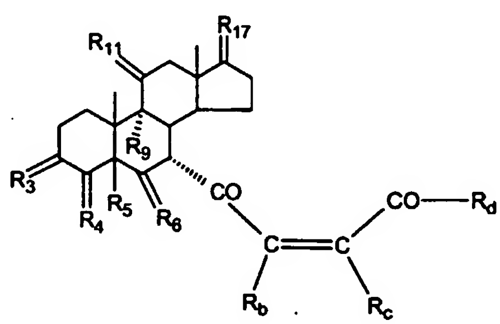
R_{S-5} is –H, C_1-C_4 alkyl, –φ;

with an acid of pK_a of < about 2.

Also disclosed is a process for purifying a 7α-substituted steroid of formula (II) where R_3, R_4, R_5 and R_6 are as defined for the 7α-substituted steroid (II) and where R_{7-1}, R_9, R_{11} and R_{17} are as defined above; which comprises:

(1) crystallizing 7α-substituted steroid (II) which contains greater than 5% of 7β-isomer from a solvent selected from the group consisting of ethyl acetate, propyl acetate and butyl acetate.

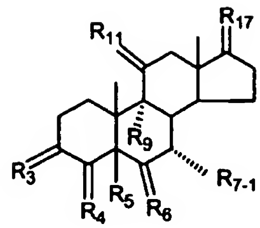
Further disclosed is a process for the preparation of a *cis*-enedione of formula (III-*cis*)



(III-cis)

where R_3, R_4, R_5 and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_{7-1}, R_{7-2}, R_9, R_{11}, R_{17}, R_b, R_c, R_d are as defined above; which comprises:

(1) contacting a 7α-substituted steroid of formula (II)



(II)

where R_3, R_4, R_5, R_6, $R_{7\text{-}1}$, R_9, R_{11} and R_{17} are as defined above; with an agent selected from the group consisting of:

(a) a halogenating agent in the presence of water and a base whose conjugate acid has a pK_a of > about 8,

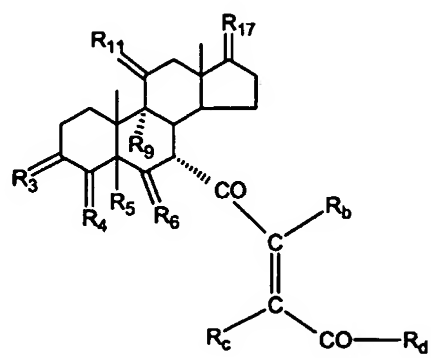
(b) an oxygen donating agent,

(c) electrochemical oxidation,

(d) a quinone in the presence of water or

(e) nonquinone oxidants.

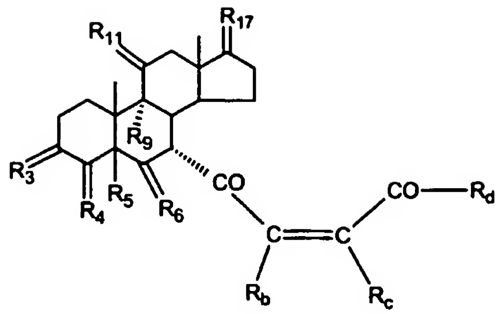
Additionally disclosed is a process for the preparation of a *trans*-enedione of formula (III-*trans*)



(III-trans)

where R_3, R_4, R_5 and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_9, R_{11}, R_{17}, R_b, R_c and R_d are as defined above; which comprises:

(1) contacting a *cis*-enedione of formula (III-*cis*)



(III-cis)

where R_3, R_4, R_5, R_6, R_9, R_{11}, R_{17}, R_b, R_c and R_d are as defined above with an isomerization catalyst selected from the group consisting of:

(a) a strong acid of pK_a of < about 2;

(b) a tertiary amine whose conjugate acid has a pK_a > about 8 and

(c) salt of a tertiary amine whose conjugate acid has a pK_a > about 8,

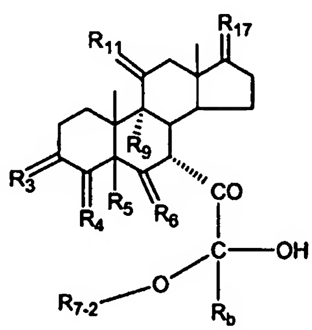
(d) I_2,

(e) $(C_1\text{-}C_4)_3P$,

(f) φ_3P,

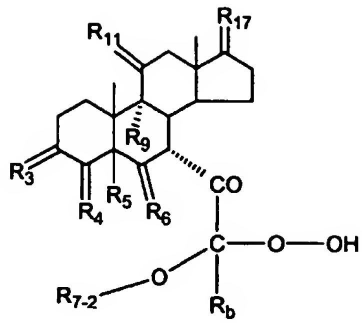
(g) heating to about 80°.

Disclosed is a process for the preparation of a hydroxy compound of formula (IV-OH)



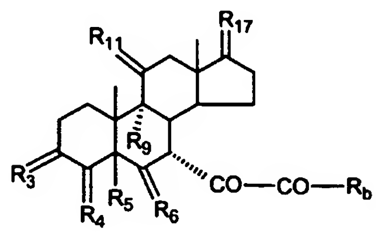
(IV-OH)

or a hydroperoxy compound of formula (IV-OOH)



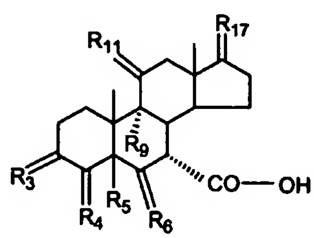
(IV-OOH)

or a biscarbonyl compound of formula (V)



(V)

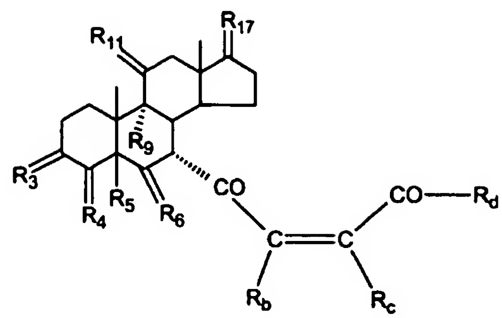
or a carboxylic acid of formula (VI)



(VI)

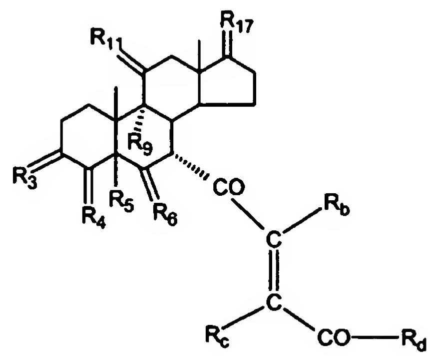
or a mixture thereof, where R_3, R_4, R_5 and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_{7-2}, R_9, R_{11}, R_{17}, R_b are as defined above; which comprises:

(1) contacting a *cis*-enedione of the formula (III-*cis*)



(III-cis)

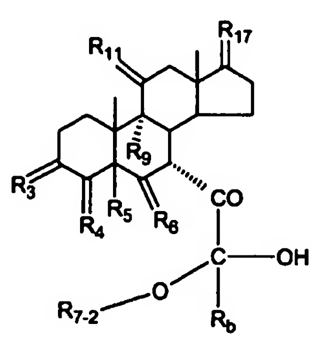
or a *trans*-enedione of the formula (III-*trans*)



(III-trans)

or a mixture thereof, where R_3, R_4, R_5, R_6, R_9, R_{11}, R_{17}, R_b, R_c and R_d are as defined above, with ozone in the presence of an alcohol of the formula $R_{7\text{-}2}$-OH, where $R_{7\text{-}2}$ is as defined above.

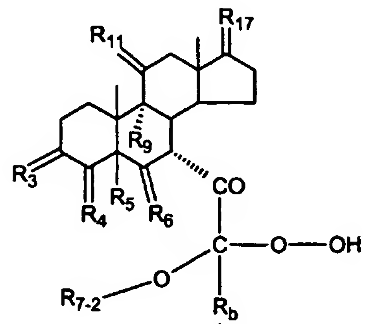
Also disclosed is a process for the preparation of a hydroxy compound of formula (IV-OH)



(IV-OH)

where R_3, R_4, R_5 and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where $R_{7\text{-}2}$, R_9, R_{11}, R_{17} and R_b are as defined above; which comprises:

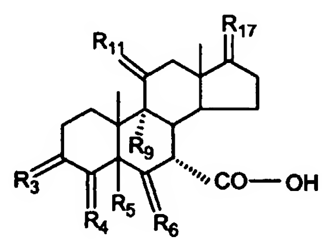
(1) contacting a hydroperoxy compound of formula (IV-OOH)



(IV-OOH)

where R_3, R_4, R_5, R_6, R_9, R_{11}, R_{17}, R_b and R_{7-2} are as defined above with a hydroperoxy-deoxygenating agent.

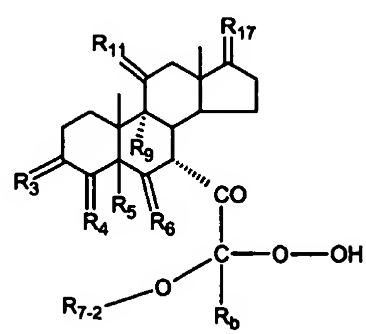
Further disclosed is a process for the preparation of a carboxylic acid of formula (VI)



(VI)

or pharmaceutically acceptable salt thereof, where R_3, R_4, R_5 and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_9, R_{11} and R_{17} are as defined above; which comprises:

(1) contacting a hydroperoxy compound of formula (IV-OOH)



(IV-OOH)

where R_3, R_4, R_5, R_6, R_9, R_{11}, R_1 R_b and R_{7-2} are as defined above; with a carboxylic acid forming agent selected from the group consisting of:

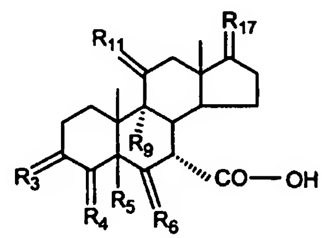
(a) heat,

(b) a base whose conjugate acid has a pK_a of about 5 or above,

(c) an acid which has a pK_a of less than about 3,

(d) an acylating agent.

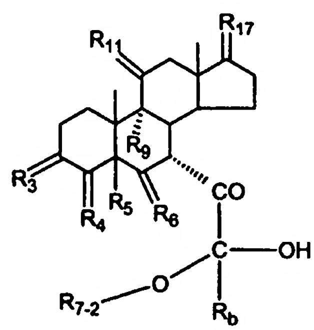
Additionally disclosed is a process for the preparation of a carboxylic acid of formula (VI)



(VI)

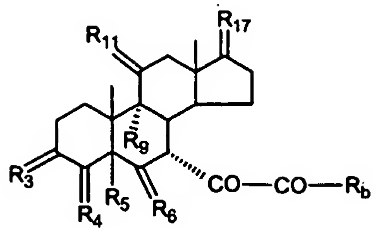
where R_3, R_4, R_5 and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_9, R_{11} and R_{17} are as defined above; which comprises:

(1) contacting a hydroxy compound of formula (IV-OH)



(IV-OH)

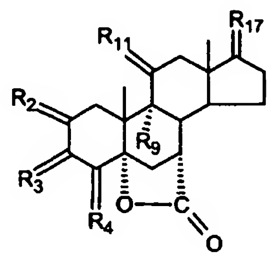
or a biscarbonyl compound of formula (V)



(V)

or mixture thereof, where R_3, R_4, R_5 and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_9, R_{11}, R_{17} and R_b are as defined above; with an oxidatively cleaving agent.

Disclosed is a process for the preparation of a 5,7-lactone of formula (VII)



(VII)

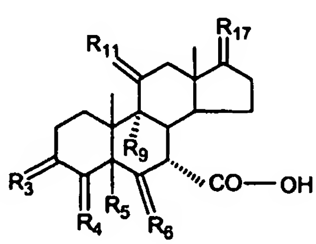
where

(Va) R_2 is –H:-H; R_3 is = O; R_4 is –H:-H;

(Vb) R_2 is –H:-H; R_3 is R_{3a}:R_{3b} where both R_{3a} and R_{3b} are –OH and R_4 is –H:-H;

where R_9, R_{11} and R_{17}, are as defined above; which comprises:

(1) contacting a carboxylic acid of formula (VI)



(VI)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is $-O-R_{31}$ and R_{3-6} is $-O-R_{32}$ where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached $-O-C-O-$ to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

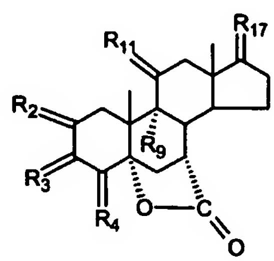
where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are $-H$ and C_1-C_3 alkyl; R_4 is $-H$:$-H$; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is $-H$;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is $-O-R_{31}$ and R_{3-8} is $-O-R_{32}$ where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is $-H$; R_6 is $-H$:$-H$;

where R_9, R_{11} and R_{17} are as defined above; with a reaction medium which has a pH of less than about 5.

Also disclosed is a process for the preparation of a 5,7-lactone of formula (VII)



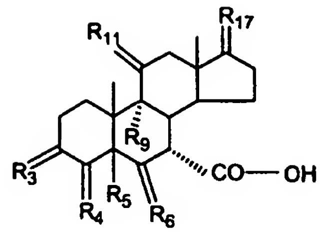
(VII)

where

(Va) R_2 is $-H$:$-H$, R_3 is $=O$ and R_4 is $-H$:$-H$;

where R_9, R_{11} and R_{17} are as defined above; which comprises:

(1) contacting a carboxylic acid of formula (VI)



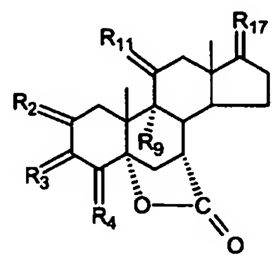
(VI)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

where R_9, R_{11} and R_{17} are as defined above; under anhydrous conditions with an anhydrous reaction medium of pH less than about 5.

Disclosed is a process for the preparation of a 5,7-lactone of formula (VII)



(VII)

where

(Vc) R_2 is –H:-H, R_3 is –O-R_{3a}:-O-R_{3b} where R_{3a} and R_{3b} the same and are C_1-C_3 alkyl or where R_{3a} and R_{3b} are taken together with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

-(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)-

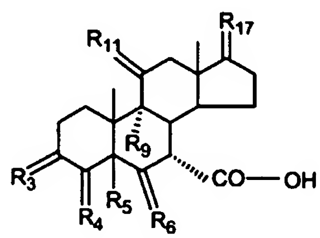
where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl, and R_4 is –H:-H;

(VI) R_2 is –H:-H; R_3 is R_{3c}:R_{3d} and R_4 is R_{4c}:R_{4d} where one of R_{3c} and R_{3d} is taken with one of R_{4c} or R_{4d} to form a second bond between the carbon atoms to which they are attached and the other of R_{3c} and R_{3d} is CH_3-O- or C_2H_5-O-; and the other of R_{4c} and R_{4d} is –H; or

(VII) R_2 is R_{2e}:R_{2f} and R_3 is R_{3e}:R_{3f} where one of R_{2e} and R_{2f} is taken with one of R_{3e} or R_{3f} to form a second bond between the carbon atoms to which they are attached and the other of R_{2e} and R_{2f} is –H, and the other of R_{3e} and R_{3f} is CH_3-O- or C_2H_5-O-; or mixtures thereof;

where R_9, R_{11} and R_{17} are as defined above;



(VI)

where

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

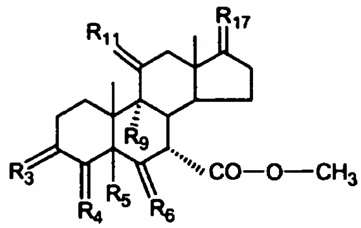
where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9, R_{11} and R_{17} are as defined above; with at least a catalytic amount of acid.

Disclosed is a process for the preparation of a methyl ester of formula (VIII)



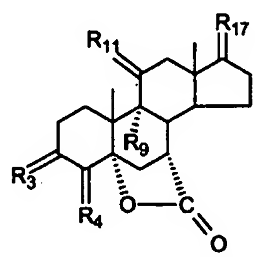
(VIII)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

where R_9, R_{11} and R_{17} are as defined above; which comprises:

(1) contacting a 5,7-lactone of the formula (VII)

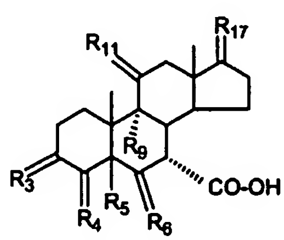


(VII)

where R_4 is –H:-H and where R_3, R_9, R_{11} and R_{17} are defined above, with base, and

(2) contacting the reaction mixture of step (1) with a methylating agent.

Also disclosed is a process for the preparation of a carboxylic acid of the formula (VI)



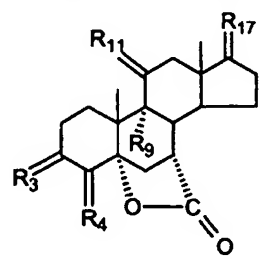
(VI)

or pharmaceutically acceptable salts there of, where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

where R_9, R_{11}, R_{17} are as defined above; which comprises:

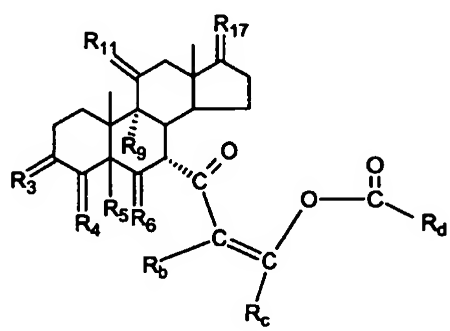
(1) contacting a 5,7-lactone of formula (VII)



(VII)

where R_4 is –H:-H; and where R_3, R_9, R_{11} and R_{17} are as defined above, with a reaction medium which as a pH > 7.

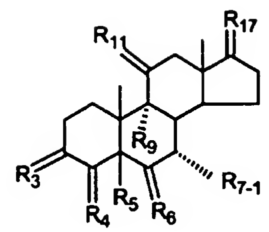
Further disclosed is a process for the preparation of a *cis*-oxyenedione of the formula (X-*cis*)



(X-cis)

where R_3, R_4, R_5, and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_9, R_{11}, R_{17}, R_b, R_c and R_d are as defined above; which comprises:

(1) contacting a 7α-substituted steroid of formula (II)

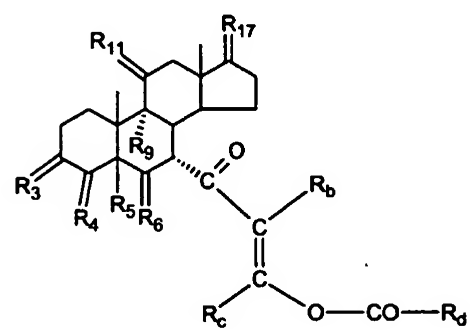


(II)

where R_3, R_4, R_5, and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where $R_{7\text{-}1}$, R_9, R_{11} and R_{17} are as defined above; with ozone in the presence of a C_1-C_4 alcohol and

(2) contacting the mixture of step (1) with a hydroperoxy-deoxygenating agent.

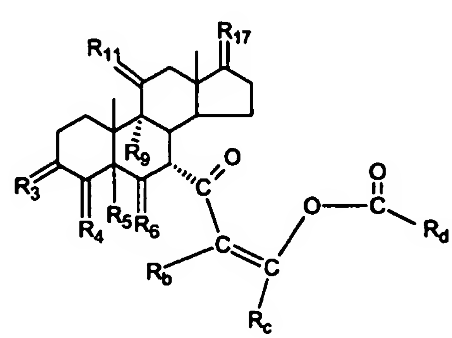
Additionally disclosed is a process 355. A process for the preparation of a *trans*-oxyenedione of the formula (X-*trans*)



(X-trans)

where R_3, R_4, R_5, and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_9, R_{11}, R_{17}, R_b, R_c and R_d are as defined above; which comprises:

(1) contacting a *cis*-oxyenedione of the formula (X-*cis*)



(X-cis)

where R_3, R_4, R_5, R_6, R_9, R_{11}, R_{17}, R_b, R_c and R_d are as defined above, with

an isomerization catalyst selected from the group consisting of:

(a) a strong acid of pK_a of < about 2;

(b) a tertiary amine whose conjugate acid has a pK_a > about 8 and

(c) salt of a tertiary amine whose conjugate acid has a pK_a > about 8,

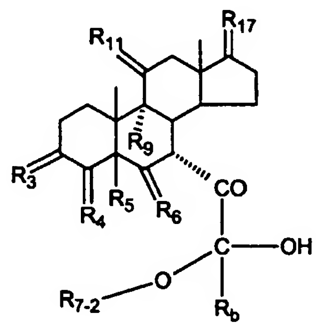
(d) I_2,

(e) $(C_1\text{-}C_4)_3P$,

(f) φ_3P,

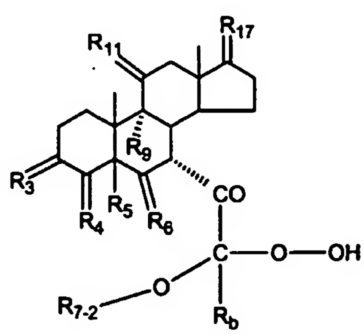
(e) heating to about 80°.

Disclosed is a process for the preparation of a hydroxy compound of formula (IV-OH)



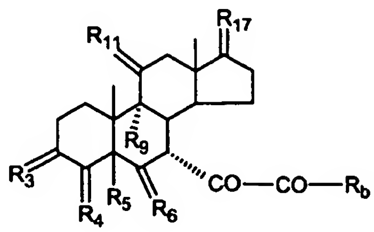
(IV-OH)

where R_3, R_4, R_5, and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where $R_{7\text{-}2}$, R_9, R_{11}, R_{17} and R_b are as defined above; or a hydroperoxy compound of formula (IV-OOH)



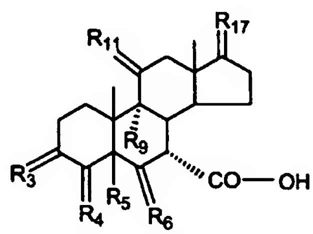
(IV-OOH)

where R_3, R_4, R_5, R_6, R_{7-2}, R_9, R_{11}, R_{17} and R_b are as defined above, or a biscarbonyl compound of formula (V)



(V)

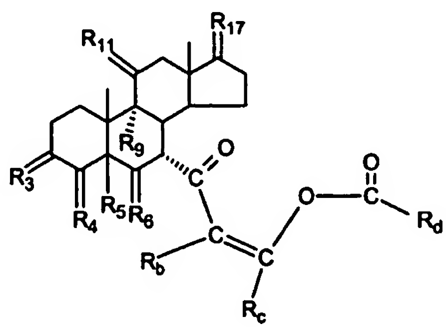
where R_3, R_4, R_5, R_6, R_9, R_{11}, R_{17} and R_b are as defined above, or a carboxylic acid of formula (VI)



(VI)

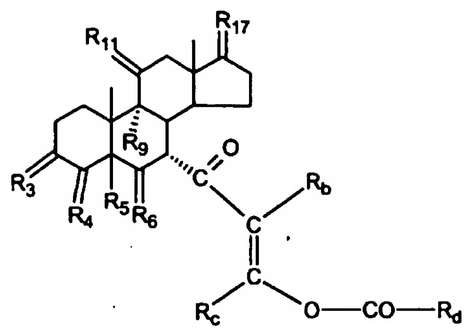
where R_3, R_4, R_5, R_6, R_9, R_{11} and R_{17} are as defined above, or a mixture thereof, which comprises:

(1) contacting an oxyenedione of the formula (X-*cis*)



(X-cis)

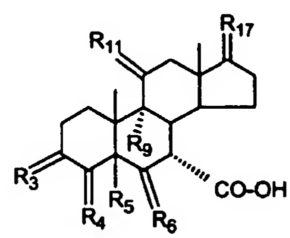
where R_3, R_4, R_5, R_6, R_9, R_{11}, R_{17}, R_b, R_c and R_d are as defined above or an oxyenedione of the formula (X-*trans*).



(X-trans)

where R_3, R_4, R_5, R_6, R_9, R_{11}, R_{17}, R_b, R_c and R_d are as defined above or mixture there of, with ozone in the presence of an alcohol of the formula R_{7-2}-OH where R_{7-2} is as defined above.

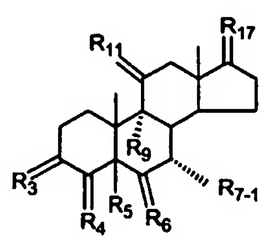
Also disclosed is a process to prepare a carboxylic acid of formula (VI)



(VI)

or salt thereof where R_3, R_4, R_5, and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_9, R_{11} and R_{17} are as defined above; which comprises:

(1) contacting a 7α-substituted steroid of formula (II)



(II)

where R_3, R_4, R_5, and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_{7-1}, R_9, R_{11} and R_{17}, are as defined above; with an agent selected from the group consisting of:

(a) a halogenating agent in the presence of water and a base whose conjugate acid has a pK_a of > about 8,

(b) an oxygen donating agent,

(c) electrochemical oxidation,

(d) a quinone in the presence of water or

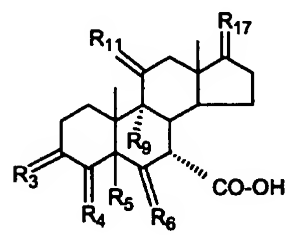
(e) nonquinone oxidants; and

(2) contacting the reaction mixture of step (1) with ozone in the presence of an alcohol of the formula R_{7-2}-OH where R_{7-2} is as defined above;

(3) contacting the reaction mixture of step (2) with a hydroperoxy deoxygenating agent and

(4) contacting the reaction mixture of step (3) with an oxidatively cleaving agent.

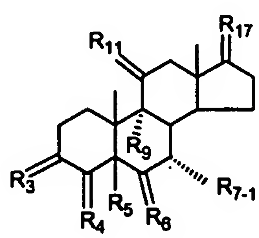
Disclosed is a process to prepare a carboxylic acid of formula (VI)



(VI)

or salt thereof where R_3, R_4, R_5, and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_9, R_{11} and R_{17} are as defined above; which comprises:

(1) contacting a 7α-substituted steroid of formula (II)



(II)

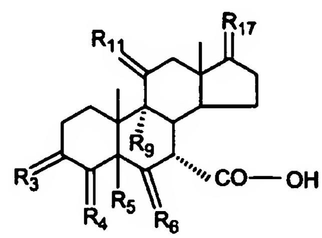
where R_3, R_4, R_5, and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_{7-1}, R_9, R_{11}, R_{17} are as defined above with

(1) ozone in the presence of an alcohol of the formula R_{7-2}-OH where R_{7-2} is as defined above;

(2) contacting the reaction mixture of step (1) with a hydroperoxy deoxygenating agent and

(3) contacting the reaction mixture of step (2) with an oxidatively cleaving agent.

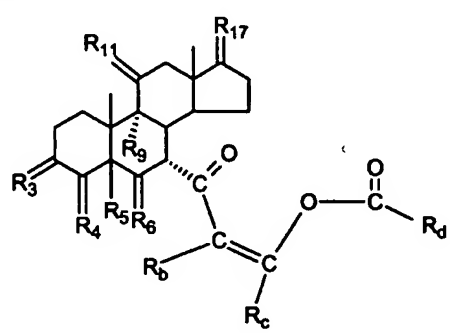
Also disclosed is a process for the preparation of a carboxylic acid of formula (VI)



(VI)

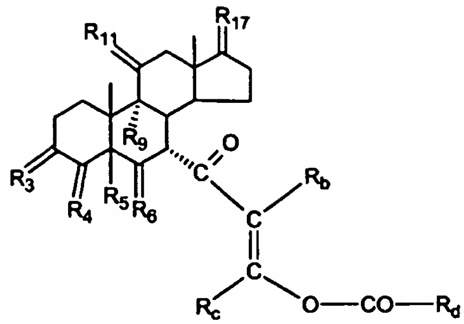
where R_3, R_4, R_5, and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_9, R_{11} and R_{17} are as defined above, which comprises:

(1) contacting a cis oxyenedione of the formula (X-*cis*)



(X-cis)

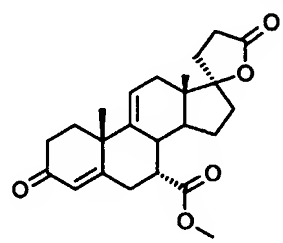
or a trans oxyenedione of the formula (X-*trans*)



(X-trans)

or mixture thereof where R_3, R_4, R_5, and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_9, R_{11}, R_{17}, R_b, R_c and R_d are as defined above, with an oxidatively cleaving agent.

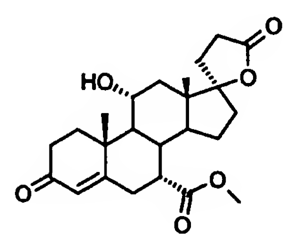
Also disclosed is a process for the preparation of a $\Delta^{9(11)}$-17-lactone (CII)



(CII)

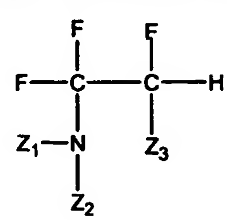
which comprises:

(1) contacting a 11α-hydroxy-17-lactone (CI)



(CI)

with a N-fluoroalkylamine reagent of formula (CVI)



(CVI)

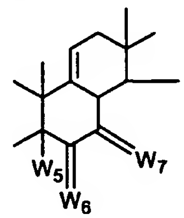
where:

Z_1 is C_1-C_4 alkyl;

Z_2 is C_1-C_4 alkyl and where Z_1 and Z_2 together with the attached nitrogen atom form a 5- or 6-member heterocycle selected from the group consisting of pyrrolidinyl, piperazinyl, piperidinyl and morpholinyl;

Z_3 is $-F$ or $-CF_3$.

Further disclosed is a process for the preparation of a $\Delta^{9(11)}$-steroid (CV)



(CV)

where W_5 is:

(1) nothing, there is a double bond between C_4 and C_5;

(2) W_6 is W_{6-1}:W_{6-2} where one of W_{6-1} or W_{6-2} is taken together with W_5 to form a second bond between the carbon atoms to which they are attached and the other of W_{6-1} and W_{6-2} is $-H$;

(3) W_5 is α-O- and W_7 is α-W_{7-1}:β-W_{7-2} where W_{7-1} is $-CO-$ resulting in a lactone (-O-CO-) with the oxygen atom bonded to the C-5 position in the α-configuration and the carbonyl group bonded to the C-7 position in the α-configuration, W_{7-2} is $-H$;

where W_6 is:

(1) -H;-H;

(2) is W_{6-3}:W_{6-4} where one of W_{6-3} and W_{6-4} is taken together with W_5 to form a double bond between C-5 and C-6 and the other of W_{6-3} and W_{6-4} is $-H$;

(3) is W_{6-3}:W_{6-4} and W_7 is W_{7-3}:W_{7-4} where one of W_{6-3} and W_{6-4} is taken together with one of W_{7-3} or W_{7-4} to form a double bond between C-6 and C-7, the other of W_{6-3} and W_{6-4} is $-H$, the other of W_{7-3} and W_{7-4} is $-H$;

where W_7 is:

(1) α-W_{7-5}:β-W_{7-6} where W_{7-5} is:

(a) $-H$,

(b) $-C\equiv N$,

(c) $-C\equiv C-H$,

(d) $-CH=CH-CH_3$,

(e) $-CO-OH$,

(f) $-CO-OW_{7-5A}$ where W_{7-5A} is:

(i) C_1-C_4 alkyl,

(ii) $-\varphi$ optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy,

(g) $-\varphi$ optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy,

(h) $-CO-SW_{7-5A}$ where W_{7-5A} is as defined above,

(i) $-CO-CH=CH-O-CO-W_{7-5A}$ where W_{7-5A} is as defined above,

(j) $-CO-CO-H$,

(k) $-CH_2-NO_2$,

(l) $-S-CO-W_{7-5A}$ where W_{7-5A} is as defined above,

(m) 5-methylfur-2-yl,

(n) 5-*t*-butylfur-2-yl,

and W_{7-6} is $-H$;

(3) α-W_{7-7}:β-W_{7-8} where W_{7-7} is $-H$ and W_{7-8} is:

(a) $-H$,

(b) $-O-CO-(C_1$-C_4 alkyl),

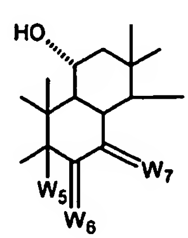
(c) $-O-CO-OW_{7-8A}$ where W_{7-8A} is:

(i) C_1-C_4 alkyl,

(ii) $-\varphi$ optionally substituted with optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy,

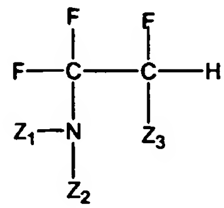
(iii) $-CH_2-\varphi$ where $-\varphi$ is optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy; which comprises:

(1) contacting a 11α-hydroxy steroid (CIV)



(CIV)

where W_5, W_6 and W_7 are as defined above, with a N-fluoroalkylamine reagent of the formula (CVI)



(CVI)

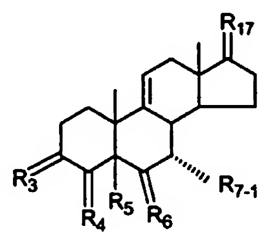
where:

Z_1 is C_1-C_4 alkyl;

Z_2 is C_1-C_4 alkyl and where Z_1 and Z_2 together with the attached nitrogen atom form a 5- or 6-member heterocycle selected from the group consisting of pyrrolidinyl, piperazinyl, piperidinyl and morpholinyl;

Z_3 is –F or –CF_3.

Additionally disclosed is a process for the preparation of a $\Delta^{9(11)}$-7α-substituted steroid of the formula (II)



(II)

where R_{17} is

(1) =O;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-$(CH_2)_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

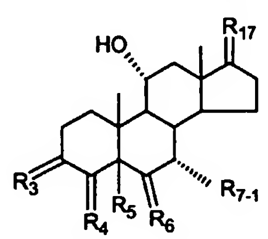
(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the

attachment of the CH_2- is at $R_{17\text{-}7}$ in the α-orientation and the attachment of the –O is at $R_{17\text{-}8}$ in the β-orientation;

(6) –O-CH($OR_{17\text{-}9}$)-CH_2-CH_2······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where $R_{17\text{-}9}$ is –H or C_1-C_3 alkyl;

(7) α-$R_{17\text{-}11}$:β-$R_{17\text{-}12}$ where $R_{17\text{-}10}$ is –$(CH_2)_{1\text{-}2}$-CH=CH_2 and $R_{17\text{-}12}$ is –OH;

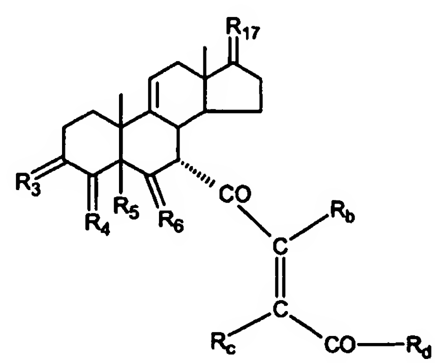
where R_3, R_4, R_5, and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where $R_{7\text{-}1}$ is as defined above, which comprises contacting a 11α-hydroxy 7α-substituted steroid of the formula (II)



(II)

where R_3, R_4, R_5, R_6 $R_{7\text{-}1}$ and R_{17} are as defined above, with a N-fluoroalkylamine reagent of formula (CVI).

Disclosed is a process for the preparation of a $\Delta^{9(11)}$-trans enedione of the formula (III-*trans*)



(III-trans)

where R_{17} is:

(1) =O;

(3) α-$R_{17\text{-}3}$:β-$R_{17\text{-}4}$ where $R_{17\text{-}3}$ is –OH and where $R_{17\text{-}4}$ is:

(a) $-CO-CH_3$,

(b) $-CO-CH_2-OH$,

(c) $-CO-CH_2-O-CO-(CH_2)_{0-3}-CH_3$;

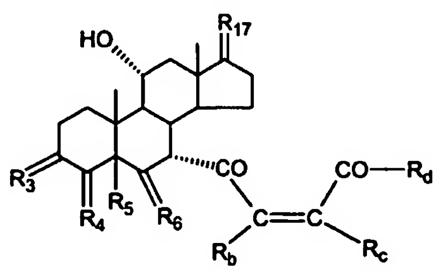
(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing $-O-CH_2-$ where the attachment of the $-O$ is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the $-O$ is at R_{17-8} in the β-orientation;

(6) $-O-CH(OR_{17-9})-CH_2-CH_2\cdots\cdots$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group ($CH_2\cdots\cdots$) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is $-H$ or C_1-C_3 alkyl;

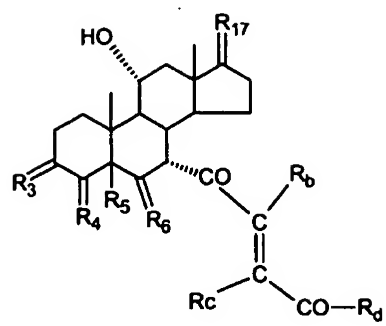
(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}-CH=CH_2$ and R_{17-12} is $-OH$;

where R_3, R_4, R_5, and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where R_b, R_c and R_d are as defined above, which comprises contacting a 11α-hydroxy cis enedione of the formula (III-*cis*)



(III-cis)

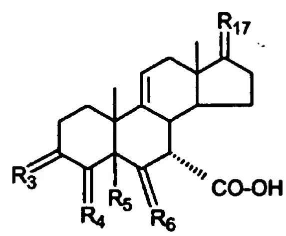
or a 11α-hydroxy trans enedione of the formula (III-*trans*)



(III-trans)

where R_3, R_4, R_5, R_6, R_{17}, R_b, R_c and R_d are as defined above, with a N-fluoroalkylamine reagent of formula (CVI).

Also disclosed is a process to prepare a $\Delta^{9(11)}$-carboxylic acid of the formula (VI)



(VI)

or salt thereof where R_{17} is:

(1) =O;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-$(CH_2)_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

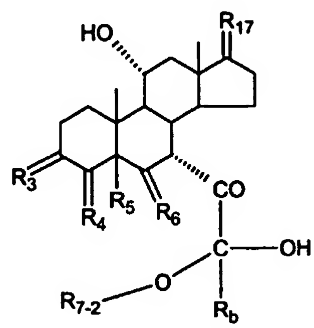
(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR$_{17-9}$)-CH$_2$-CH$_2$$\cdots\cdots$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH$_2$$\cdots\cdots$) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R$_{17-9}$ is –H or C$_1$-C$_3$ alkyl;

(7) α-R$_{17-11}$:β-R$_{17-12}$ where R$_{17-10}$ is –(CH$_2$)$_{1-2}$-CH=CH$_2$ and R$_{17-12}$ is –OH;

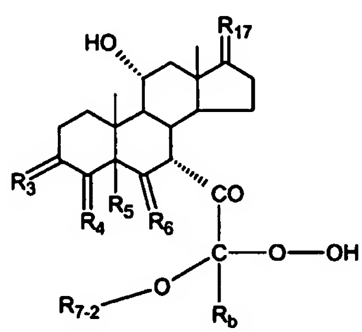
where R$_3$, R$_4$, R$_5$, and R$_6$ are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*), which comprises

(1) contacting a 11α-hydroxy-hydroxy compound of the formula (IV-OH)



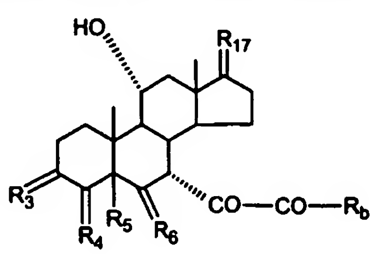
(IV-OH)

or a 11α-hydroxy-hydroperoxy compound of the formula (IV-OOH)



(IV-OOH)

or a 11α-hydroxy biscarbonyl compound of the formula (V)



(V)

where R_3, R_4, R_5, and R_6 are as defined for the *cis* and *trans* enedione (III-*cis*) and (III-*trans*) and where $R_{7\text{-}2}$, R_{17} and R_b, are as defined above, with a N-fluoroalkylamine reagent of formula (CVI) and

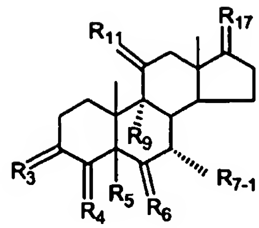
(2) contacting the reaction mixture of step (1) with an oxidatively cleaving agent.

DETAILED DESCRIPTION OF THE INVENTION

Eplerenone is 9α,11α-epoxy-17β-hydroxypregn-4-en-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester and as such contains a 7α-carbomethoxy substituent. It is useful as a pharmaceutical agent for the treatment of hypertension and congestive heart failure. A major difficulty in the production of eplerenone is introduction of the 7α-carbomethoxy substituent. The processes and intermediates of the present invention are improved processes for the preparation of eplerenone.

CHART A discloses the general process of the invention when the adduct at the 7α-position, $-R_{7\text{-}1}$ is (-A1). The process of the present invention begins with a protected or unprotected $\Delta^{4,6}$-3-keto steroid (I). Since the steroid A-ring can be protected or not protected, CHART B discloses an improved process for protection of the $\Delta^{4,6}$-3-keto steroid (I) starting material as a C-3 protected $\Delta^{4,6}$-3-ketal steroid (I-P). CHART C discloses an alternative route (ozonolysis) for transformation of the 7α-substituted steroid (II) to eplerenone (IX). CHART D discloses the general process when the steroid A-ring is unprotected and $R_{7\text{-}1}$ is the variable substituent (-A1). CHART E discloses the preferred process for the transformation of a $\Delta^{4,6}$-3-keto steroid or ketal thereof (I) to eplerenone (IX). CHART F discloses the reversible nature of the conversion of the carboxylic acid (VI) with the 5,7-lactone (VII). CHART G discloses the general process of the invention when $-R_{7\text{-}1}$ is (-A2). CHART H discloses the general process of the invention when $-R_{7\text{-}1}$ is (-B), (-C), (-D1), (-D2) or (-D3).

The first step in the process of CHART A is to prepare a 7α-substituted steroid (II) of the formula



(II)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(II) R_3 is R_{3-3}:R_{3-4} and R_4 is R_{4-3}:R_{4-4} where one of R_{3-3} and R_{3-4} is –O-R_{31} where R_{31} is C_1-C_3 alkyl, the other of R_{3-3} and R_{3-4} is taken together with one of R_{4-3} and R_{4-4} to form a second bond between the carbon atoms to which they are attached, and the other of R_{4-3} and R_{4-4} is –H; R_6 is R_{6-3}:R_{6-4} where one of R_{6-3} and R_{6-4} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-3} and R_{6-4} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

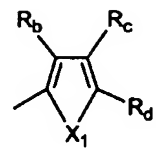
$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

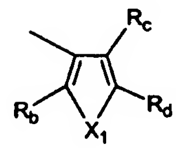
(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_{7-1} is a molecular fragment of the formula (-A1)



(-A1)

or of the formula (-A2)



(-A2)

where X_1 is:

–S-,

-O- or

$-NX_{1-1}$- and where X_{1-1} is:

-H,

C_1-C_4 alkyl,

-CO-OX_{1-2} where X_{1-2} is C_1-C_4 alkyl or –CH_2-φ,

-CO-X_{1-2} where X_{1-2} is as defined above,

-CO-φ where –φ is substituted in the *o*-position with –CO-O-(C_1-C_4 alkyl),

-SO_2-(C_1-C_3 alkyl),

-SO_2-φ where φ is optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

–CO-OCH$_3$ and

-CO-R$_{c-1}$ where R$_{c-1}$ is C_1-C_4 alkyl or –φ;

where R$_d$ is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl;

C_1-C_4 alkoxy;

-CH$_2$-OR$_{d-1}$ where R$_{d-1}$ is –H or C_1-C_4 alkyl,

-CH$_2$-N(R$_{d-6}$)$_2$ where the two R$_{d-6}$ are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R$_{d-6a}$ where R$_{d-6a}$ is C_1-C_4 alkyl or –φ,

-CH$_2$-O-CO-R$_{d-1}$ where R$_{d-1}$ is as defined above,

-CH(OR$_{d-1}$)$_2$ where R$_{d-1}$ is as defined above and where the two R$_{d-1}$ taken together are:

-CH$_2$-CH$_2$-,

-CH$_2$-CH$_2$-CH$_2$-,

-CH$_2$-C(CH$_3$-)$_2$-CH$_2$-,

-CH(-O-CO-R$_{d-1}$)$_2$ where R$_{d-1}$ is as defined above,

-Si(R)$_3$ where R is as defined above,

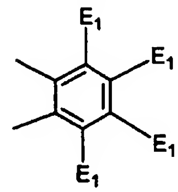
-O-Si(R)$_3$ where R is as defined above,

-Sn(R$_{b-1}$)$_3$ where R$_{b-1}$ is as defined above,

-S-R$_{d-5}$ where R$_{d-5}$ is C_1-C_4 alkyl or –φ,

-N(R$_{d-6}$)$_2$ where R$_{d-6}$ is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

-OE_{1-1} where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

–$SiE_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

-S-E_{1-5} where E_{1-5} is C_1-C_4 alkyl or –φ,

-S-$(O)_{1-2}$-E_{1-5} where E_{1-5} is as defined above,

-$N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are as defined above,

-P(O)(O-E_{1-1})$_2$ where E_{1-1} is as defined above,

-$Si(R)_3$ where R is as defined above;

-CE_1=M (-B)

where E_1 is as defined above and

where M is:

(1) =O,

(2) =N-E_2 where E_2 is selected from the group consisting of

-H

C_1-C_4 alkyl,

C_1-C_4 alkenyl containing 1 or 2 double bonds,

C_1-C_4 alkynyl containing 1 triple bond,

-CO-OE_{2-1} where E_{2-1} is –H or C_1-C_4 alkyl,

-$C(E_{2-1})_2$-OE_{2-2} where E_{2-1} are the same or different and are as defined above and where E_{2-2} is

C_1-C_4 alkyl,

-φ or

–$Si(R)_3$ where the three R are the same or different and are defined above,

-OE_{2-2} where E_{2-2} is as defined above,

-S-E_{2-3} where E_{2-3} is C_1-C_4 alkyl or –φ,

-S-$(O)_{1-2}$-E_{2-3} where E_{2-3} is as defined above,

-$N(R_{d-6})_2$ where the two R_{d6} are the same or different and are as defined above;

-$Si(R)_3$ where the three R are as defined above;

(3) =$C(E_2)_2$ where the E_2 are the same or different and are as defined above,

where E_1 and E_2 are taken together with the atoms to which they are attached to form a ring of 5 thru 7 members, optionally containing 3 thru 5

–O-,

-S-,

–N=,

-NX_{1-1}- where X_{1-1} is as defined above,

-CE_2= where E_2 is as defined above,

-$C(R_b)_2$- where R_b is as defined above, and optionally containing 1 or 2 additional double bonds;

-C≡C-E_2 (-C)

where E_2 is as defined above;

-CH_2-CH=CH_2 (-D1)

-CH=C=CH_2 (-D2)

-CH_2-C≡C-H (-D3)

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of

$-Si(-CH_3)_3$,

$-Si(-CH_2-CH_3)_3$,

$-CO-CH_3$,

-CO-H and

$-SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above, and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above, with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) $-C\equiv C-H$,

(c) $-C\equiv N$,

(d) $-C\equiv C-CH_2-O-R_{17-1-1}$ where R_{17-1-1} is selected from the group consisting of

(i) $-H$,

(ii) $-Si(R_{17-1-2})_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) $-C\equiv C-CH_2-O-$(HYDROXY PROTECTING GROUP), where HYDROXY PROTECTING GROUP is as defined above,

(f) $-CH_2-CH_2-CH_2-OH$,

(g) $-CH_2-CH_2-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) $-CH_2-CH_2-CO-O^-$ and where R_{17-2} is $-OH$;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is $-OH$ and where R_{17-4} is:

(a) $-CO-CH_3$,

(b) $-CO-CH_2-OH$,

(c) $-CO-CH_2-O-CO-(CH_2)_{0-3}-CH_3$;

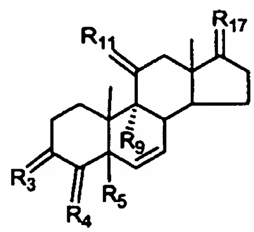
(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing $-O-CH_2-$ where the attachment of the $-O$ is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the $-O$ is at R_{17-8} in the β-orientation;

(6) $-O-CH(OR_{17-9})-CH_2-CH_2\cdots\cdots$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group ($CH_2\cdots\cdots$) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is $-H$ or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH; which comprises:

(1) contacting a $\Delta^{4,6}$-3-keto steroid or ketal thereof (I) of the formula



(I)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached;

(I-ketal) R_3 is R_{3-9}:R_{3-10} where R_{3-9} is –O-R_{31} and R_{3-10} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

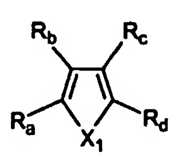
$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is R_{4-9}:R_{4-10} where one of R_{4-9} and R_{4-10} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-9} and R_{4-10} is –H;

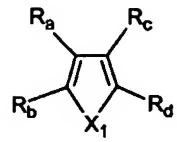
where R_9, R_{11} and R_{17} are as defined above, with an adduct selected from compounds

(a) of the formula (A)



(A1)

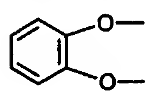
or



(A2)

where X_1, R_b, R_c and R_d are as defined above, and

where R_a is selected from the group consisting of –H, -ZnL, -BL, -SiL_3, -SnL_3, -Cu, -CuL, -AlL_2, -HgL, -Ag, -MgL, -Li and –COOH, where L is –OH, C_1-C_4 alkyl, -F, -Cl, -Br, -I, -CN, -O(C_1-C_3 alkyl), 2-thienyl, $(CH_3)_2C(O\text{-})\text{-}C(O\text{-})C(CH_3)_2$ and

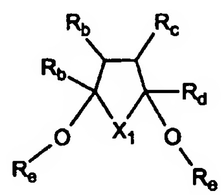

;

(b) of the formula (A')

$$R_b\text{-CO-CHR}_b\text{-CHR}_c\text{-CO-}R_d \qquad (A')$$

where R_b, R_c and R_d are as defined above;

(c) of the formula (A'')



(A")

where R_e is:

C_1-C_4 alkyl,

-CO-(C_1-C_4 alkyl or –φ),

-$Si(R)_3$ where R is as defined above and where X_1, R_b, R_c and R_d are as defined above;

(d) of the formula (B)

$$R_a\text{-CE}_1\text{=M} \qquad (B)$$

where R_a, E_1 and M are as defined above;

(e) of the formula (C)

$$R_a\text{-C}\equiv\text{C-}E_2 \qquad (C)$$

where R_a and E_2 are as defined above;

(f) of the formulas (D1, D2 and D3)

$$R_a\text{-CH}_2\text{-CH=CH}_2 \qquad (D1)$$

$$R_a\text{-CH=C=CH}_2 \qquad (D2)$$

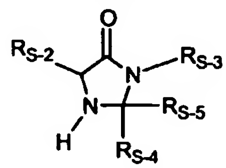
$$R_a\text{-}CH_2\text{-}C{\equiv}C\text{-}H \quad (D3)$$

where R_a is as defined above, in the presence of:

(1) a Lewis Acid,

(2) a proton acid with a pK_a of < about 5 or

(3) a salt of a secondary amine of the formula



where

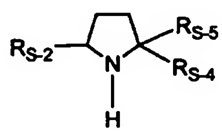
R_{S-2} is –H, C_1-C_4 alkyl, –φ, and -CH_2-φ;

R_{S-3} is –H, C_1-C_4 alkyl;

R_{S-4} is –H, C_1-C_4 alkyl, –φ;

R_{S-5} is –H, C_1-C_4 alkyl, –φ;

and



where

R_{S-2} is –H, C_1-C_4 alkyl, –φ, and -CH_2-φ;

R_{S-4} is –H, C_1-C_4 alkyl, –φ;

R_{S-5} is –H, C_1-C_4 alkyl, –φ;

with an acid of pK_a of < about 2.

For the Δ^4-3-keto or ketal thereof (I) starting material it is preferred that R_3, R_4 and R_5 are (I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

For the 7α-substituted steroid (II), there were four sets of steroid A-/B-rings identified above. Groups (I), (III) and (IV) are operable in the processes of the present invention. However, group (II) where R_3 is R_{3-3}:R_{3-4} and R_4 is R_{4-3}:R_{4-4} where one of R_{3-3} and R_{3-4} is –O-R_{31} where R_{31} is C_1-C_3 alkyl, the other of R_{3-3} and R_{3-4} is taken together with one of R_{4-3} and R_{4-4} to form a second bond between the carbon atoms to

which they are attached, and the other of R_{4-3} and R_{4-4} is –H; R_6 is R_{6-3}:R_{6-4} where one of R_{6-3} and R_{6-4} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-3} and R_{6-4} is –H; is a $\Delta^{3,5}$-3,3-dialkoxy ring system which, as such, can not be transformed to the other intermediates of the present invention. It is useful because it can be transformed to the corresponding Δ^4-3-keto steroid A-/B-ring system which is useful in the processes of the present invention.

For the 7α-substituted steroid (II) and other steroidal compounds of the invention, except the 5,7-bislactone (VII), with regard to the steroidal A-/B-rings, it is preferred that R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

For the 7α-substituted steroid (II) and other steroidal compounds of the invention, except the 5,7-bislactone (VII), with regard to the steroidal A-/B-rings, it is more preferred that R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

With regard to the steroidal C-ring, it is preferred that R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H. It is more preferred that R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

With regard to the steroidal D-ring, it is preferred that R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation,

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH,

(d) –C≡C-CH_2-O-R_{17-1-1}.

With regard to the 7α-substituted steroid (II), it is preferred that R_{7-1} is substituent of formula (-A1). It is also preferred that X_1 is –O-. It is preferred that R_b and R_c are –H and it is preferred that R_d is C_1 alkyl. It is preferred that R_a is –H. It is preferred that for R_a that L is

-ZnL is -Cl, -Br, -I;

-BL is catecholate,

two –OH,

HO-CH_2-CH_2-OH,

HO-CH_2-CH_2-CH_2-OH,

HO-CH_2-C$(CH_3)_2$-CH_2-OH;

-SiL_3 is C_1 alkyl;

-SnL_3 is C_1 or *n*-C_4 alkyl;

-CuL is 2-thienyl or –CN and

$-AlL_2$ is C_1-C_2 alkyl.

When R_a is Cu, there can be two R_a groups for one Cu in which case the Cu is anionic.

The preferences for the variable substituents R_3, R_4, R_5, R_6, R_{7-1}, R_9, R_{11}, R_{17}, R_a, R_b, R_c, R_d and X_1 are not just for the $\Delta^{4,6}$-3-keto steroid or ketal thereof (I) and/or the 7α-substituted steroid (II), but rather are for all the compounds (I) thru (XV) of the invention, except as expressly noted. Similarly, the preferences for other variable substituents such as R_{7-2} discussed below and/or chemical reagents used in this patent such as oxygen donating agent, halogenating agent, isomerization catalyst, hydroperoxy-deoxygenating agent, acid forming agent, acylation catalyst, oxidatively cleaving agent, deoxygenating agent, are defined the same throughout the patent as the first time they are discussed. Since many of these variable substituents and chemical reagents are referred to numerous times, it would be redundant each time they are used to repeatedly mention what is included, what is preferred and more preferred.

It is preferred that the acid reactant be a Lewis acid. The Lewis acid must be electrophilic enough to complex with the $\Delta^{4,6}$-3-keto steroid or ketal thereof (I), but not so electrophilic that it complexes with the nucleophilic reagent (A1) , (A2), (B), (C), (D1), (D2) or (D3) as is known to those skilled in the art. Further, it is preferred that the Lewis Acid be used in the presence of an alcohol selected from the group consisting of C_1-C_3 alcohols, ethylene glycol, 1,2- or 1,3-propylene glycol, 2,2-dimethyl- or 2,2-diethyl-1,3-propylene glycol and phenol. It is more preferred that the alcohol be a C_1-C_3 alcohol or mixture thereof. Useful Lewis acids include those selected from the group consisting of

BX_3, AlX_3, SnX_2, SnX_4, SiX_4, MgX_2, ZnX_2, TiX_4,

$Rh(acac)(CH_2CH_2)_2$(2,2'-bis(diphenylphosphino)-1,1'-binaphthyl),

$Rh(CH_3\text{-}C{\equiv}N)_2$(cyclooctadiene)$(BF_4)$,

$Rh(acac)(CH_2CH_2)_2$(dppb),

$LiClO_4$,

K10 Montmorillonite clay,

$Yb(OTf)_3$,

$LiCo(B_9C_2H_{11})_2$,

PdX_2,

CrX_3,

FeX_3,

CoX_3,

NiX_2,

SbX_5,

InX_3,

$Sc(OTf)_3$,

$\varphi_3C^+X^-$

$(R)_3SiX$ where R is C_1-C_4 alkyl and $-\varphi$; where X is selected from the group consisting of F^-, Cl^-, Br^-, I^-, $-O-SO_2CF_3^-$, PF_6^-, BF_4^-, and ClO_4^-;

$Pd(CH_3-CO-O^-)_2$;

BF_3-diethyletherate complex;

BF_3-acetic acid complex;

BF_3-methyl-*t*-butyl ether complex;

BF_3-di-*n*-butyletherate complex;

BF_3-dimethyletherate complex;

BF_3-dimethylsulfide complex;

BF_3-phenol complex;

BF_3-phosphoric acid complex and

BF_3-tetrahydrofuran complex. It is preferred that the Lewis acid is selected from the group consisting of BF_3, BF_3-diethyletherate complex, BF_3-acetic acid complex, BF_3-methyl-*t*-butyl ether complex, BF_3-di-*n*-butyletherate complex, BF_3-dimethyletherate complex, BF_3-dimethylsulfide complex, BF_3-phenol complex, BF_3-phosphoric acid complex and BF_3-tetrahydrofuran complex. It is more preferred that the Lewis acid is BF_3-diethyletherate. It is even more preferred that the BF_3-diethyletherate is used in the presence of C_1-C_3 alcohol and still more preferred is the use of the BF_3-diethyletherate in the presence of C_2 alcohol. Useful acids with a pK_a of < about 5 are selected from the group consisting of formic acid, acetic acid, propionic acid, benzoic acid, acid, hydrofluoric acid, fluoroboric acid, *p*-toluenesulfonic acid, methanesulfonic acid, benzenesulfonic acid, trifluoromethanesulfonic acid, perchloric acid, trifluoroacetic and trichloroacetic. It is preferred that the acid with a pK_a of < about 5 is acetic acid. When performing the

transformation of the $\Delta^{4,6}$-3-keto steroid or ketal thereof (I) to the corresponding 7α-substituted steroid (II), at least one equivalent of the reagent of formulas (A), (B) or (C) should be used, it is preferable to use from one to two equivalents. Use of additional reagent is not a problem, but rather a waste of compound. The reaction can be carried out in a variety of solvents, such as in a solvent/solvent mixture selected from the group consisting of:

C_1-C_6 alcohols,

a solvent mixture of C_1-C_6 alcohols and a solvent selected from the group consisting of acetonitrile, nitromethane, toluene, methylene chloride and acetic acid. One factor to be considered in selecting a Lewis acid and solvent is the acid sensitivity of the 7α-substituted steroid (II). The reaction must be performed with a Lewis acid and in a solvent where the product is stable as is known to those skilled in the art. It is preferred that the solvent be a protic solvent, one that has a pK_a of less than about 19. The reaction can be performed in a temperature range of from about -78° to about 60°; preferably in a temperature range of from about -40° to about -15°. It is more preferred to perform the reaction at about –20°. The reaction normally will take from a few hours to a day depending on the number of equivalent used and the reaction temperature.

Useful 7α-substituted steroids (II) include those selected from the group consisting of:

17β-hydroxy-7α-(5'-methyl-2'-furyl)-pregna-4,9-dien-3-one-21-carboxylic acid, γ-lactone,

11α,17β-dihydroxy-7α-(5'-methyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone,

9α,11α-epoxy-17β-hydroxy-7α-(5'-methyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone,

17β-hydroxy-7α-(5'-t-butyl-2'-furyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone,

11α,17β-dihydroxy-7α-(5'-t-butyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone,

11α,17β-dihydroxy-7α-(4'-bromo-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone,

11α,17β-dihydroxy-7α-(4'-methyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone and

7α-allyl-17β-hydroxypregna-4,9(11)-dien-3-one, 21-carboxylic acid, γ-lactone.

Rather than carrying the 7α-substituted steroid (II) on to the next step *in situ*, it is preferred to isolate and purify the 7α-substituted steroid (II) before performing the next step. The preferred method of purification of the 7α-substituted steroid (II) is by crystallization. The process for purifying the 7α-substituted steroid of formula (II) comprises crystallizing the 7α-substituted steroid (II), which contains greater than 5% of the 7β-isomer from a solvent selected from the group consisting of ethyl acetate, *n*-propyl acetate and butyl acetate. It is preferred to obtain the 7α-substituted steroid (II) in greater than 99.8% isomeric purity and it is preferred that the crystallization solvent is *n*-propyl acetate. Crystallization co-solvents may be used.

The next step in the process of CHART A, is the conversion of the 7α-substituted steroid (II) to the corresponding *cis*-enedione (III-*cis*), by an oxidative process which comprises (1) contacting the 7α-substituted steroid of formula (II) with an agent selected from the group consisting of:

(a) a halogenating agent in the presence of water and a base whose conjugate acid has a pK_a of > about 8,

(b) an oxygen donating agent,

(c) electrochemical oxidation,

(d) a quinone in the presence of water or

(e) nonquinone oxidants. It is preferred that the agent be a halogenating agent. Useful halogenating agents include those selected from the group consisting of dibromodimethylhydantoin, dichlorodimethylhydantoin, diiododimethylhydantoin, N-chlorosuccinamide, N-bromosuccinamide, N-iodosuccinamide, trichloroisocyanuric acid, *t*-butylhypochlorite and 3-bromo-1-chloro-5,5-dimethylhydantoin; it is preferred that the halogenating is dibromodimethylhydantoin. When using a halogenating agent, the amount used should be at least one equivalent of the halogenating agent; preferably from about 1.0 to about 1.05 equivalents of the halogenating agent are used. It is more preferred that the amount of halogenating agent be about 1.01 equivalents. The reason is that one equivalent is required to complete the reaction but any excess needs to be quenched. Suitable quenching agents include bisulfite,

isobutylvinyl ether, 2-methylfuran and hypophosphorous acid. Useful oxygen donating agents include those selected from the group consisting of:

a peracid,

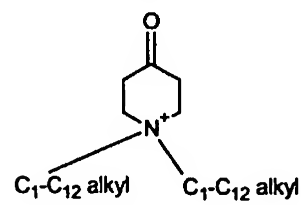
singlet oxygen followed by either phosphite or thiourea,

triplet oxygen,

hydrogen peroxide with a ketone selected from the group consisting of Q_4-CO-Q_5 where Q_4 and Q_5 are the same or different and are:

C_1-C_4 alkyl optionally substituted with 1 thru 9 –Cl or –F, and where the

Q_4 and Q_5 are taken together with the attached carbon atom to form a cyclic ketone of 5 thru 7 members and ketones of the formula:



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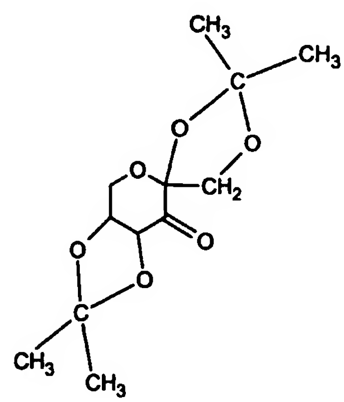


hydrogen peroxide in combination with methyltrioxorhenium,

trichloroacetonitrile/hydrogen peroxide,

trichloroacetamide/hydrogen peroxide,

DDQ/water,

p-chloranil/water,

φ-$C(CH_3)_2$-O-OH or an alkylhydroperoxide in combination with a metal containing activator, where alkyl is from C_4-C_{10} alkyl and metal containing activator is selected from the group consisting of Ti(isopropoxide)$_4$, peroxotungstophosphate, VO(acetylacetonate)$_2$ and MO hexacarbonyl. It is preferred that the oxygen donating agent is a peracid. Useful peracids include those selected from the group consisting of:

(a) perbenzoic acid optionally substituted with 1 or 2 –Cl or –NO_2,

(b) percarboxylic acids of the formula $C_{n2}(Q_6)2_{n2+1}$-CO_3H where n_2 is 1 thru 4 and Q_6 is –H, -Cl or –F,

(c) perphthalic acid and

(d) magnesium peroxyphthalate. An excess oxygen donating agent present must also be quenched as was done for the halogenating agents. Base is required to neutralize the acid produced during the transformation of the 7α-substituted steroid (II) to the *cis*-enedione (III-*cis*). Use bases include those selected from the group consisting of acetate, bicarbonate, carbonate, propionate, benzoate, dibasic phosphate and borate; it is more preferred that the base be acetate. For example, when the halogenating agent is dibromodimethylhydantoin, hydrobromic acid is produced. Hence, one equivalent of base per equivalent of acid produced is required. In practice, a slight excess is used, about 1.5 equivalents. Suitable solvents for this reaction are those which are water miscible and which dissolves both the 7α-substituted steroid (II) and the halogenating agent or oxygen donating agent. Acetone and THF are preferred solvents. The reaction is performed at room temperature, about 20 to about 25°. The reaction takes a few hours depending on the reactivity of the oxygenating donating agent or halogenating agent. When formed, the *cis*-enedione (III-*cis*) does not have to be isolated and purified, but rather can be used in subsequent transformations "as is" or *in situ*. It is preferred that the *cis*-enedione (III-*cis*) is 17β-hydroxy-7α-(*cis*-1',4'-dioxopent-2'-en-1'yl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone. Other oxidants useful for transformation of the 7α-substituted steroid (II) to the *cis*-enedione (III-*cis*) include quinones (listed elsewhere). The 7α-substituted steroid (II) is contacted with a stoichiometric amount of quinone and at least a stoichiometric amount of water in a water-miscible organic solvent. The contacting is preferably done at around room temperature. In addition, the oxidation can be accomplished by

electrochemistry. The electrochemical oxidation is accomplished by contacting the 7α-substituted steroid (II) with a sub-stoichiometric amount of a quinone (preferably DDQ) and at least a stoichiometric amount of water in an electrochemical cell using standard electrochemical techniques such as are described in US 4,270,994. Finally, the oxidation can be accomplished with non-quinone agents which include, manganic acetate, potassium permanganate, ceric ammonium nitrate, iodosobenzene, iodobenzenediacetate, iodobenzenebistrifluoroacetate, chromic acid ("Jones reagent"), and lead tetraacetate. These reactions are typically run in aqueous acetone as solvent at around room temperature (20-25°), although many water-miscible organic co-solvents can be used in place of acetone. Other oxidizing agents that effect this transformation include hydrogen peroxide or an organic hydroperoxide (listed elsewhere) in combination with a metal catalyst such as methyltrioxorhenium, palladium acetate, ruthenium trichloride, or ruthenium tetroxide. These reactions can be run in any solvent in which the 7α-substituted steroid (II) is soluble such as methylene chloride, acetone, etc. The reactions involving ruthenium catalysts are preferably run in aqueous acetonitrile.

In the process of CHART A, the *cis*-enedione (III-*cis*) can be transformed to the corresponding *trans*-enedione (III-*trans*) or it can be converted to the peroxy compound (IV-OOH), the hydroxy compound (IV-OH), the biscarbonyl compound (V) or the carboxylic acid (VI) or mixture thereof. When the term carboxylic acid (VI) is used, it refers to and includes the pharmaceutically acceptable salts thereof. These will include the sodium, potassium, lithium, magnesium, tetrabutylammonium and the carboxylic acid salts with DBU, tetramethylquanidine, triethylamine and others. The identity of the particular cation is not important since eventually it is lost when forming an acid which ultimately is converted to the methyl ester (VIII) and eplerenone (IX) which requires a methyl ester at the 7α-position. It is preferable to convert the *cis*-enedione (III-*cis*) to the corresponding *trans*-enedione (III-*trans*) rather than convert the *cis*-enedione (III-*cis*) to a mixture of peroxy (IV-OOH), hydroxy (IV-OH) and biscarbonyl (V) compounds.

When the *cis*-enedione (III-*cis*) is transformed to the corresponding *trans*-enedione (III-*trans*), the *cis*-enedione (III-*cis*) is contacted with an isomerization catalyst which can be either a chemical agent including:

(a) a strong acid of pK_a of < about 2;

(b) a tertiary amine whose conjugate acid has a pK_a > about 8 and

(c) salt of a tertiary amine whose conjugate acid has a pK_a > about 8,

(d) I_2,

(e) $(C_1\text{-}C_4)_3P$,

(f) φ_3P, or a physical agent such as

(g) heating to about 80°.

It is preferred that the isomerization catalyst be a strong acid of pK_a of < about 2. When the isomerization catalyst is a strong acid of pK_a of < about 2, useful strong acids of pK_a of < about 2 include those selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodoic acid, hydrofluoroic acid, sulfuric acid, phosphoric acid, nitric acid, trichloroacetic acid and trifluoroacetic acid, it is preferred that the strong acid of pK_a of < about 2 be hydrochloric acid. When the isomerization catalyst is a strong acid of pK_a of < about 2, it is preferred that it be used in anhydrous form or if used in as an aqueous mixture that the reaction be performed as a two phase system with the aqueous phase being separate. When the isomerization catalyst is a tertiary amine whose conjugate acid has a pK_a > about 8, useful tertiary amines whose conjugate acid has a pK_a > about 8 include those selected from the group consisting of $(Q_3)_3N$ were Q_3 is C_1-C_3 alkyl, DBU, DBN, DABCO, pyridine, *p*-dimethylaminopyridine and pyrrolidinylpyridine. When the isomerization catalyst is salt of a tertiary amine whose conjugate acid has a pK_a > about 8, it is preferred that the salt of a tertiary amine whose conjugate acid has a pK_a > about 8 be pyridine hydrochloride. Regardless of which chemical agent is used, only a catalytic amount is required. For example, after formation of the *cis*-enedione (III-*cis*) just adding commercial chloroform containing the usual impurity of hydrochloric acid is sufficient to effect the transformation to the corresponding *trans*-enedione (III-*trans*), see EXAMPLE 4, Part 2. The isomerization of *cis*-enedione (III-*cis*) to the corresponding *trans*-enedione (III-*trans*) can be performed at 20-25° (room temperature). At room temperature, the reaction usually takes a few hours. It is necessary to monitor the course of the reaction by standard methods such as LC or TLC to ensure that it does not go too long. If the reaction goes too long, the reaction reforms the 7α-substituted steroid (II) with a Δ^6-double bond. Once the reaction has

proceeded to completeness where it is desirous to terminate the reaction, the reaction can be terminated as follows. When the isomerization catalyst is an acid or salt of a tertiary amine whose conjugate acid has a pK_a of > 8, one can terminate the reaction by washing with water. If aqueous acid is used as the isomerization catalyst, it is best to separate the phases and then wash the non-aqueous phase with water. If the isomerization catalyst is a tertiary amine whose conjugate acid has a pK_a of > 8, then the reaction mixture is washed with aqueous acid followed by water. The *trans*-enedione (III-*trans*) can be isolated and purified, however it is preferred not to isolate and purify it but rather carry it on *in situ*.

In the process of CHART A, the next step is the conversion of either the *cis*-enedione (III-*cis*) or *trans*-enedione (III-*trans*), or mixture thereof, to the corresponding hydroperoxy (IV-OOH) compound, hydroxy (IV-OH) compound, biscarbonyl (V) compound and/or the carboxylic acid (VI) or mixtures thereof. The *cis*-enedione (III-*cis*) or *trans*-enedione (III-*trans*), or mixture there of, is transformed to the corresponding hydroxy compound, peroxy compound (IV-OOH), or biscarbonyl compound (V) or carboxylic (VI) by contacting the *cis*-enedione (III-*cis*) or *trans*-enedione (III-*trans*) or a mixture thereof, with ozone in the presence of an alcohol of the formula R_{7-2}-OH where R_{7-2} is –H or C_1-C_4 alkyl optionally substituted with one or two –OH. This includes water, methanol, ethanol, propyl alcohol, isopropyl alcohol, ethylene glycol, glycerol, etc. It is preferred that R_{7-2} is –H, C_1 or is iso-C_3; it is more preferred that R_{7-2} is a mixture of –H, C_1 and iso-C_3. This means a mixture of water, methanol and isopropanol is the preferred R_{7-2}-OH. The steroidal starting materials must be in solution using a solvent that will dissolve them at the cold temperatures at which it is preferred to perform this reaction. Methylene chloride is the preferred solvent. The reaction temperatures can be as low as about –100° up to about 40°. It is preferred that the temperature be from about –78° to about –20°; it is more preferred that the temperature be about –50°. The lower the temperature, the more selectivity; the higher the temperature the less selectivity. Hence, the actual temperature used will depend on the particular reactants used and the degree of selectivity desired. The reaction is permitted to run until the starting material is reduced to a small amount. The ozone must be stopped when the starting material is consumed or the ozone will destroy the product by reacting with the Δ^4- and/or $\Delta^{9(11)}$-

double bonds if present. The alcohol, R_{7-2}-OH, is used in a large excess to efficiently trap the carbonyl oxide intermediate produced. Further, the reaction temperature, the time the reaction is permitted to run and the nature of the particular alcohol, R_{7-2}-OH, determines the identity of the product or if more than one product is produced, the ratio of products. If the alcohol, R_{7-2}-OH, has a hindered R_{7-2} group, then the product is more likely to be the biscarbonyl compound (V), all other things being equal. Similarly, if the alcohol, R_{7-2}-OH, does not have a hindered R_{7-2} group, such as methyl, then the product is more likely to be the hydroxy compound (IV-OH), all other things being equal. The preferred product produced by the oxidation process is the carboxylic acid (VI).

The hydroperoxy compound (IV-OOH) can be converted to the corresponding hydroxy compound (IV-OH) by contacting the hydroperoxy compound (IV-OOH) with a hydroperoxy-deoxygenating agent. It is preferred to use a mild hydroperoxy-deoxygenating agent, one which both deoxygenates, and second does not add to the steroid molecule. Useful hydroperoxy-deoxygenating agents include those selected from the group consisting of:

Q_1Q_2S where Q_1 and Q_2 are the same or different and are C_1-C_4 alkyl or phenyl,

bisulfite,

sulfite,

thiosulfate,

tetrahydrothiophene,

hydrosulfite,

thiourea,

butyl vinyl ether,

(C_1-C_4 alkyl)$_3$ phosphine,

triphenylphosphine, and

tetramethylethylene. It is preferred that the hydroperoxy-deoxygenating agent is dimethylsulfide. When the hydroperoxy-deoxygenating agent is bisulfite and sulfite, sodium and potassium are the preferred cations. One equivalent of the hydroperoxy-deoxygenating agent is required, but more then one equivalent, such as about two equivalents, are normally used to ensure that all of the hydroperoxy

compound (IV-OOH) is reduced. The reaction is performed at 20-25° and is usually complete in about 1 hour. The hydroxy compound (IV-OH) can be isolated and purified if desired, however, it is preferable to carry it on *in situ* without isolating or purifying it. It is preferred that the hydroxy compound (IV) is 17β-hydroxy-7α-(1'-oxo-2'-isopropoxy-2'-hydroxy-ethyl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone.

The hydroperoxy compound (IV-OOH) can be transformed to the corresponding carboxylic acid (VI) by contacting the hydroperoxy compound (IV-OOH) with a carboxylic acid forming agent selected from the group consisting of:

(a) heat,

(b) a base whose conjugate acid has a pK_a of about 5 or above,

(c) an acid which has a pK_a of less than about 3,

(d) an acylating agent. When the carboxylic acid forming agent is (a) heat, the reaction mixture should be heated to the range of from about 30° to about 120°; preferably from about 80° to about 90°. When the carboxylic acid forming agent is, (b) a base whose conjugate acid has a pK_a of about 5 or above, useful bases include inorganic bases selected from the group consisting of hydroxide, bicarbonate, and carbonate and organic bases selected from the group consisting of $(Q_3)_3N$ were Q_3 is C_1-C_3 alkyl, DBU, DBN, DABCO, pyridine and *p*-dimethylaminopyridine. It is preferred that the base is bicarbonate. Sufficient base is necessary to neutralize the steroid acid produced and any additional acid by-products. When the carboxylic acid forming agent is, (c) an acid which has a pK_a of less than about 3, useful acids include those selected from the group consisting of hydrochloric acid, sulfuric acid, phosphoric acid, nitric acid and organic acids of the formula of R_{acid-1}-COOH where R_{acid-1} is –H and C_1-C_3 alkyl optionally substituted with 1 thru 3 –Cl and –F; preferred are formic acid and trifluoroacetic acid. While catalytic amounts of acid are sufficient, several equivalent are preferred. When the carboxylic acid forming agent is, (d) an acylating agent, useful acylating agents are selected from the group consisting of R_{acid-2}-CO-O-CO-R_{acid-2} where R_{acid-2} is

–H,

C_1-C_3 alkyl optionally substituted with 1 thru 3 –Cl and -F and

-φ. It is preferred that acylating agent is acetic anhydride or trifluoracetic anhydride. One equivalent of the acylating agent is required. When using an acylating agent, it is preferred to use it with an acylation catalyst. Preferred acylation catalysts are pyridine and *p*-dimethylaminopyridine (DMAP). With regard to solvents, it is important to perform the process under homogenous reaction conditions to avoid decomposition of the hydroperoxy compound (IV-OOH). This means using one phase conditions. Therefore, the solvent of choice will depend on the carboxylic acid forming agent used. If the carboxylic acid forming agent requires water to dissolve the reagent such as when the carboxylic acid forming agent is bicarbonate, then a water miscible organic solvent such as acetone, methanol, DMF or isopropanol is required. If the carboxylic acid forming agent is pyridine then the organic solvent can be a water immiscible organic solvent such as acetonitrile, methylene chloride or ethyl acetate. Hence, the selection of the solvent depends on the nature of the carboxylic acid forming agent used as is know to those skilled in the art. With the exception of the carboxylic acid forming agent (a) heat, the other acid forming agents (b), (c) and (d) can all be reacted at 20-25°. The reaction is quite fast and is usually over in less than one hour.

Both the hydroxy compound (IV-OH) and the biscarbonyl compound (V) are converted to the corresponding carboxylic acid (VI) in the same manner. The process involves contacting the hydroxy compound (IV-OH) or the biscarbonyl compound (V), or mixture thereof, with an oxidatively cleaving agent. Useful oxidatively cleaving agents are selected from the group consisting of:

(1) hydrogen peroxide with a carboxylic acid forming agent selected from the group consisting of:

(a) heat,

(b) a base whose conjugate acid has a pK_a of about 5 or above,

(c) an acid which has a pK_a of less than about 3,

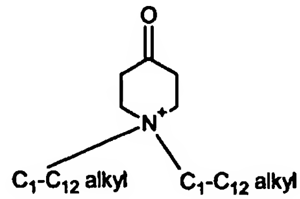
(d) an acylating agent and an acylation catalyst;

(2) $KHSO_5$;

(3) hydrogen peroxide with a ketone selected from the group consisting of Q_4-CO-Q_5 where Q_4 and Q_5 are the same or different and are:

C_1-C_4 alkyl optionally substituted with 1 thru 9 –Cl or –F,

where the Q_4 and Q_5 are taken together with the attached carbon atom to form a cyclic ketone of 5 thru 7 members, and ketones of the formula:



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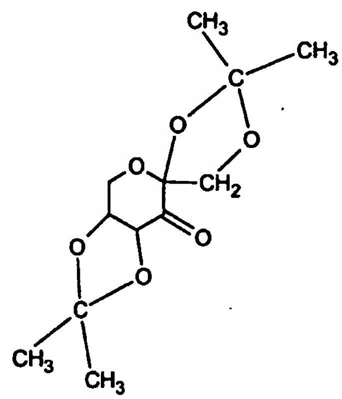


(4) hydrogen peroxide in combination with methyltrioxorhenium,

(5) φ-$C(CH_3)_2$-O-OH or an alkylhydroperoxide in combination with a metal containing activator, where alkyl is from C_4-C_{10} alkyl and metal containing activator is selected from the group consisting of Ti(isopropoxide)$_4$, peroxotungstophosphate, VO(acetylacetonate)$_2$ and Mo hexacarbonyl;

(6) peracids selected from the group consisting of

(a) perbenzoic acid optionally substituted with 1 or 2 –Cl or –NO_2,

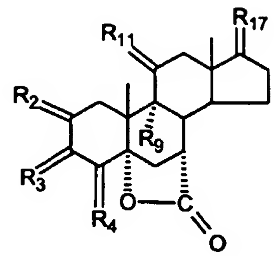
(b) percarboxylic acids of the formula $C_{n2}(Q_6)2_{n2+1}$-CO_3H where n_2 is 1 thru 4 and Q_6 is –H, -Cl or –F,

(c) perphthalic acid,

(d) magnesium peroxyphthalate. It is preferred that the oxidatively cleaving agent is hydrogen peroxide with a carboxylic acid forming agent. When the carboxylic acid forming agents are (a) heat, (b) a base whose conjugate acid has a pK_a of about 5 or above, (c) an acid which has a pK_a of less than about 3 or (d) an

acylating agent and an acylation catalyst, they should be used in the same manner as discussed above for the transformation of the hydroperoxy compound (IV-OOH) to the corresponding carboxylic acid (VI). As stated above, one equivalent of the oxidatively cleaving agent is required. Two equivalents are normally used and the reaction is monitored so that when the reaction nears completion it is stopped, or quenched, and worked up before the oxidatively cleaving agent attacks the Δ^4- and/or $\Delta^{9(11)}$-steroid double bonds. Hydrogen peroxide and bicarbonate are preferred as the oxidatively cleaving agent. With regard to solvents it is important to perform the process under homogenous reaction conditions, meaning one phase conditions. Therefore, the solvent of choice will depend on the oxidatively cleaving agent used. If the carboxylic acid forming agent requires water to dissolve the reagent such as when the carboxylic acid forming agent is bicarbonate, then a water miscible organic solvent such as acetone, DMF, methanol or isopropanol is required. If the carboxylic acid forming agent is pyridine then the organic solvent can be a water immiscible organic solvent such as acetonitrile, methylene chloride or ethyl acetate. Hence, the selection of the solvent depends on the nature of the carboxylic acid forming agent used as is known to those skilled in the art. With the exception of the carboxylic acid forming agent (a) heat, the other acid forming agents (b), (c) and (d) can all be reacted at 20-25°. The reaction is quite fast and is usually over in less than one hour. If the reaction mixture contains some hydroperoxy compound (IV-OOH), then it is useful to first treat the reaction mixture with a hydroperoxy-deoxygenating agent. It is preferred that the hydroperoxy-deoxygenating agent is dimethylsulfide.

There are a number of processes to transform a carboxylic acid (VI) to the corresponding 5,7-lactone (VII), where the C- and D-rings of the starting carboxylic acid (VI) and product 5,7-lactone are the same. The processes differ depending on the nature of the steroid A-/B-rings of the starting carboxylic acid (VI). They use different reactants and produce 5,7-lactones (VII) with different steroid A-/B-rings. One of these processes produces a 5,7-lactone of formula (VII)



(VII)

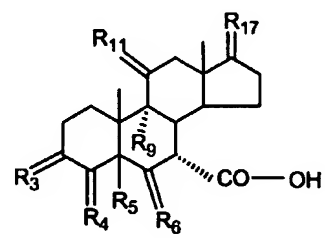
where

(Va) R_2 is –H:-H; R_3 is = O; R_4 is –H:-H;

(Vb) R_2 is –H:-H; R_3 is R_{3a}:R_{3b} where both R_{3a} and R_{3b} are –OH and R_4 is –H:-H;

where R_9, R_{11} and R_{11} are as defined above, which comprises:

(1) contacting a carboxylic acid of formula (VI)



(VI)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

-(CH$_2$)-(CR$_{33}$R$_{34}$)$_{n1}$-(CH$_2$)-

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is

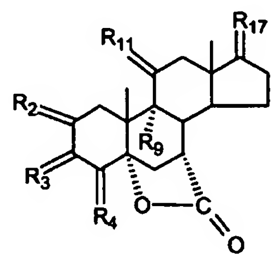
$-H:-H$; R_6 is $R_{6-5}:R_{6-6}$ where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is $-H$;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is $-O-R_{31}$ and R_{3-8} is $-O-R_{32}$ where R_{31} and R_{32} are as defined above; R_4 is $R_{4-7}:R_{4-8}$ where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is $-H$; R_6 is $-H:-H$;

where R_9, R_{11} and R_{17} are as defined above; with a reaction medium which has a pH of less than about 5. The conversion of the carboxylic acid (VI) to the corresponding 5,7-lactone (VII) is an equilibrium reaction. The lower the pH used for the reaction medium the more the equilibrium shifts toward the 5,7-lactone (VII), hence the desire to keep the pH less than 5 and preferably in the range of 1 thru 5. It is preferred to perform the reaction under anhydrous conditions; under anhydrous conditions it is preferred that the acid be a strong acid of pK_a less than about 2. Useful strong acids include those selected from the group consisting of fluorosulfonic, chlorosulfonic, benzenesulfonic, *p*-toluenesulfonic, methanesulfonic, trifluoromethanesulfonic, trifluoroacetic, trichloroacetic, hydrochloric, sulfuric, phosphoric and nitric; it is preferred that the acid is benzenesulfonic, *p*-toluenesulfonic or methanesulfonic acid. Alternatively, the process can be performed using aqueous acid as the catalyst. Under these conditions it is preferred to perform the process in a two-phase system. The amount of acid used in not very important and can be present in an amount from catalytic to excess. Bases are also operable to catalyze the reaction of the carboxylic acid (VI) to the corresponding 5,7-lactone (VII) as long as they are used in a catalytic amount. Useful bases include those selected from the group consisting of hydroxide, bicarbonate, carbonate, DBU, DBN, DABCO, pyridine, *p*-dimethylaminopyridine, Q_7-COO^- where Q_7 is $-H$, C_1-C_3 alkyl or $-\varphi$, $(Q_3)_3N$ where Q_3 is C_1-C_3 alkyl; preferred are hydroxide, bicarbonate, carbonate, triethylamine or pyridine. The solvents for the transformation of the carboxylic acid (VI) to the corresponding 5,7-lactone (VII) are helpful in effecting the equilibrium of the reaction. It is preferred to use a solvent in which the starting carboxylic acid (VI) is soluble and in which the 5,7-lactone (VII) is not soluble. That way the 5,7-lactone (VII) precipitates out as it is formed pushing the equilibrium towards the desired 5,7-

lactone (VII). A preferred solvent is acetone. This reaction is performed from about 0° to about 25° and is complete in a few hours. Depending on the pH of the reaction medium and solvent used, ratios of < 95/5 of carboxylic acid (VI)/5,7-lactone (VII) are obtained. Since this process step is an equilibrium reaction, the pH of the reaction medium helps control the final position of the equilibrium as is known to those skilled in the art.

A second process for producing a 5,7-lactone of formula (VII)



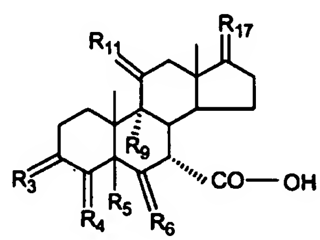
(VII) .

where

(Va) R_2 is –H:-H, R_3 is =O and R_4 is –H:-H;

where R_9, R_{11} and R_{17} are as defined above, comprises:

(1) contacting a carboxylic acid of formula (VI)



(VI)

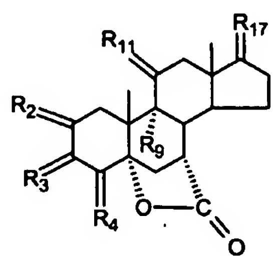
where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

where R_9, R_{11} and R_{17} are as defined above; under anhydrous conditions with an anhydrous reaction medium of pH less than about 5. It is preferred that the reaction medium contains an acid which has a pK_a of < about 4. Useful acids which have a pK_a of < about 4 include those selected from the group consisting of fluorosulfonic, chlorosulfonic, benzenesulfonic, *p*-toluenesulfonic, methanesulfonic,

trifluoromethanesulfonic, trifluoroacetic, trichloroacetic, hydrochloric, sulfuric, phosphoric and nitric. It is preferred that the acid is benzenesulfonic, *p*-toluenesulfonic or methanesulfonic. It is also preferred that the carboxylic acid (VI) is reacted with the acid in a two-phase system. The process also includes reacting the carboxylic acid (VI) with a catalytic amount of base. Useful bases include those selected from the group consisting of hydroxide, bicarbonate, carbonate, DBU, DBN, DABCO, pyridine, *p*-dimethylaminopyridine, Q_7-COO^- where Q_7 is –H, C_1-C_3 alkyl or –φ, $(Q_3)_3N$ where Q_3 is C_1-C_3 alkyl.

A third process for producing a 5,7-lactone of formula (VII)



(VII)

where

(Vc) R_2 is –H:-H, R_3 is –O-R_{3a}:-O-R_{3b} where R_{3a} and R_{3b} the same and are C_1-C_3 alkyl or where R_{3a} and R_{3b} are taken together with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl, and R_4 is –H:-H;

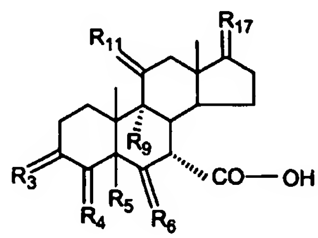
(VI) R_2 is –H:-H; R_3 is R_{3c}:R_{3d} and R_4 is R_{4c}:R_{4d} where one of R_{3c} and R_{3d} is taken with one of R_{4c} or R_{4d} to form a second bond between the carbon atoms to which they are attached and the other of R_{3c} and R_{3d} is CH_3-O- or C_2H_5-O-;
and the other of R_{4c} and R_{4d} is –H; or

(VII) R_2 is R_{2e}:R_{2f} and R_3 is R_{3e}:R_{3f} where one of R_{2e} and R_{2f} is taken with one of R_{3e} or R_{3f} to form a second bond between the carbon atoms to which they

are attached and the other of R_{2e} and R_{2f} is –H, and the other of R_{3e} and R_{3f} is CH_3-O- or C_2H_5-O-; or mixtures thereof;

where R_9, R_{11} and R_{17} are as defined above, comprises:

(1) contacting a carboxylic acid of formula (VI)



(VI)

where

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

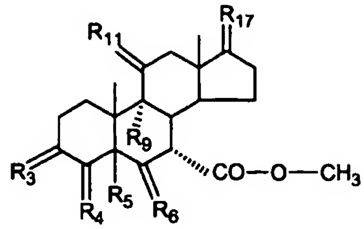
where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9, R_{11} and R_{17} are as defined above; with at least a catalytic amount of acid. It is preferred that the acid have a pK_a of < about 4 and are as discussed above.

The present invention includes a process for the preparation of a methyl ester of formula (VIII)



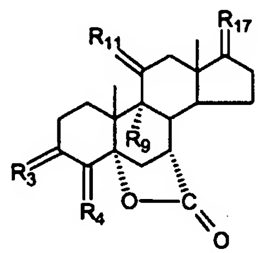
(VIII)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

where R_9, R_{11} and R_{17} are as defined above, which comprises:

(1) contacting a 5,7-lactone of the formula (VII)



(VII)

where R_4 is –H:-H and where R_3, R_9, R_{11} and R_{17} are defined above, with base, and

(2) contacting the reaction mixture of step (1) with a methylating agent.

The base needs to be strong enough to open the 5,7-lactone (VII) but of the type that will not react with the methylating agent, a weak nucleophile. Useful bases include those selected from the group consisting of bicarbonate, carbonate, hydroxide and $R_{base}O^-$ where R_{base} is C_1-C_4 alkyl. It is preferred that the base is bicarbonate. The amount of base required is from about 1 to about 1.5 equivalents. Useful methylating agents include those selected from the group consisting of dimethylsulfate, methyl iodide, methyl bromide, trimethylphosphate, dimethylcarbonate and methyl chloroformate; preferred is dimethylsulfate. The amount of methylating agent used should be the same as the number of equivalents of base used or a very slight excess over that. The preferred method of the process is to react it in a sequential manner in a two-step reaction with base first and then the methylating agent. If the reaction is performed all in one step, the base reacts with the methylating reagent necessitating

the need for more base and more methylating agent. The more efficient way is to first react the 5,7-lactone (VII) with at least one equivalent of base, preferably from about 1 to about 1.5 equivalents and then to react the salt of the carboxylate acid (VI) which is formed with the methylating agent. The solvent used will depend on the nature of the base used. If it is water soluble, such as bicarbonate or hydroxide, then a mixture of water and a water miscible organic solvent is preferred. These water miscible organic solvents include, methanol, ethanol, isopropanol, acetone, THF and DMF. If the base is water soluble and the solvent is a mixture of water and a water immiscible solvent, then a phase transfer catalyst, such as tetrabutylammonium bisulfate or tributylmethylammonium chloride is used. If the base is soluble in a water immiscible organic solvent, one that will also dissolve the 5,7-lactone (VII), then a water-immiscible organic solvent is suitable. The reaction temperature is dependent on the reactivity of the methylating agent. If an agent such as dimethylcarbonate is used the reaction will go slow and heat up to about 150° may be necessary. On the other hand, if a more reactive agent such as dimethylsulfate is used the reaction goes in about 1 hour at 40°. While in theory one equivalent of base and one equivalent of methylating agent should be sufficient, in practice more than one equivalent is needed for the optimum reaction conditions.

The 5,7-lactone (VII) can be transformed to the (salt of the) corresponding carboxylic acid (VI) by contacting the 5,7-lactone of formula (VII), with a reaction medium which as a pH > 7. The reaction is similar to the transformation of the 5,7-lactone (VII) to the methyl ester (VIII) except that no methylating agent is used. Since only base is used, the product produced is the salt of the carboxylic acid (VI). Further, since no methylating agent is present, the amount of base used is not critical. If the acid form of the carboxylic acid (VI), is desired the salt form can be acidified to produced the corresponding acid form of the carboxylic acid (VI) as is known to those skilled in the art.

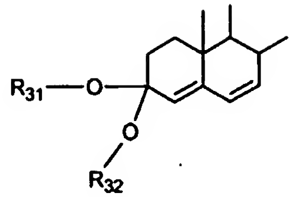
There are numerous alternative routes using the present invention as set forth in CHART A as will be explained below and is known to those skilled in the art. For example, the steroid A-ring can be protected, as compound (I-P), see CHART B and the explanation below, during the transformation of (I) to (II) or used in the unprotected form (I). Further, the C- and D-rings can have a variety of functionality

during the various steps of the process. The C-ring functionality includes, for example, 9α-hydroxy, 9α-O-(HYDROXY PROTECTING GROUP), 9α-F, 11-keto, 11-saturated, 11α-hydroxy, 11α-O-(HYDROXY PROTECTING GROUP), 11β-hydroxy, 11β-O-(HYDROXY PROTECTING GROUP), $\Delta^{9(11)}$- and 9α,11α-epoxy. The D-ring functionality includes, for example, 17-keto, 17β-hydroxy, 17α-ethynyl-17β-hydroxy, 17α-cyano-17β-hydroxy, 17α–C≡C-CH_2-O-(-H or substitutedsilyl)-17β-OH, 17α–C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) -17β-OH, 17α–CH_2-CH_2-CH_2-OH-17β-OH, 17α–CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP)-17β-OH, 17α-hydroxy-17β-CO-CH_3, 17β–CO-CH_2-OH, 17β–CO-CH_2-O-CO-$(CH_2)_{0\text{-}3}$-CH_3; 17β–O-CH_2-17α resulting in a three member epoxide, γ-lactone and –O-CH($OR_{17\text{-}9}$)-CH_2-CH_2····· where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where $R_{17\text{-}9}$ is –H or C_1-C_3 alkyl. However, the D-ring functionality for the compounds of the processes of claims 539, 548 and 556 does not include $R_{17\text{-}2}$ being hydroxyl. HYDROXY PROTECTING GROUPs are well known to those skilled in the art. The same HYDROXY PROTECTING GROUPs are operable at C-9, C-11 and C-17 and are selected from the group consisting of: -Si(-CH_3)$_3$, -Si(-CH_2-CH_3)$_3$, -CO-CH_3, -CO-H and -SiH(CH_3)$_2$.

At some point the A-ring, if it is not already the required Δ^4-3-keto functionality, must be transformed to the Δ^4-3-keto functionality. Likewise, with the C-ring, if it is not already the required 9α,11α-epoxide functionality, it must be transformed to the 9α,11α-epoxide. Similarly, if the D-ring is not already the required γ-lactone, it must be transformed to the γ-lactone. However, those transformations can take place either before, during or after various other processes and/or steps of CHART A. It is preferred to start with the A-ring with Δ^4-3-keto functionality, the C-ring with $\Delta^{9(11)}$-functionality and the D-ring as the γ-lactone. With regard to the C-ring, it is preferred to maintain the $\Delta^{9(11)}$-functionality throughout the process of the invention until the -CO-O-CH_3 group is fully synthesized at the 7α-position and then transform the $\Delta^{9(11)}$-functionality to the corresponding 9α,11α-epoxide. With regard to the C-ring one could start with a 11-keto functionality and at some point in the process reduce it to the 11α-hydroxy functionality and then at some later point

dehydrate the 11α-hydroxy functionality to the corresponding $\Delta^{9(11)}$-olefin functionality by either the processes of EXAMPLEs 18-20 using PCl_5 or by the process of EXAMPLE 31 using N-(1,1,2,2,3,3,3) hexafluoropropyldiethyl-amine which is known as Ishikawa reagent. There is a thorough discussion below as to how the dehydration of an 11α-hydroxy steroid should be performed using the Ishakawa reagent to produce the corresponding $\Delta^{9(11)}$-olefin. If the dehydration of the 11α-hydroxy to the corresponding $\Delta^{9(11)}$-olefin takes place with a 5'-methyl-2'-furyl substituent at C-7α, with a formula (II) compound, it appears PCl_5 is preferred, but if the dehydration takes place on the methyl ester (VII), then the Ishikawa reagent is preferred. The $\Delta^{9(11)}$-olefin is then converted to the desired 9α,11α-epoxide functionality by means well known to those skilled in the art. Likewise, with regard to the D-ring, one need not start with the γ-lactone in the $\Delta^{4,6}$-3-keto steroid or ketal thereof (I) starting material. One could start with 17-keto or 17β-hydroxy, etc and then at a desired point covert the starting D-ring 17-functionality to the desired γ-lactone. The preferred process including what functionality is desired to start with, and where the conversions are made, is set forth in CHART E. In short, it is desired to start with the same functionality as is desired in the end product for the A-ring and D-rings. It is preferred to start with the C-ring having the $\Delta^{9(11)}$-olefin functionality which is transformed to the desired 9α,11α-epoxide functionality after the 7α-substitutent is finalized as $-CO-O-CH_3$. However, as explained above and is known to those skilled in the art, there are numerous alternative ways of preparing eplerenone by the process of CHART A starting with different functionality in the A-, C- and D-rings.

CHART B discloses a process to produce the protected $\Delta^{4,6}$-ketal steroid (I-P), from the corresponding $\Delta^{3,5}$-3-alkyl enol ethers which are readily available from the corresponding Δ^{4}-3-keto steroids by processes known to those skilled in the art. It is preferred use the unprotected $\Delta^{4,6}$-3-keto steroid (I) as the starting material in the process of CHART A. However, steroidal $\Delta^{4,6}$-3-ketals (I-P) can also be used as the starting material of the process of CHART A. In the process of CHART B, the $\Delta^{4,6}$-3-ketal steroid (I-P)



(I-P)

where R_{31} and R_{32}

(1) the same or different and are C_1-C_3 alkyl, and

(2) taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

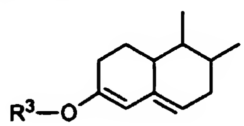
where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are

-H,

C_1-C_3 alkyl,

is produced from the corresponding $\Delta^{3,5}$-3-alkyl enol ether



(Alkyl enol ether)

where R^3 is

C_1-C_3 alkyl,

CH_3-CO-,

Φ-CO- or

$R_{Si-1}R_{Si-2}R_{Si-3}Si$- where R_{Si-1}, R_{Si-2} and R_{Si-3} are the same or different and are C_1-C_4 alkyl; by contacting the $\Delta^{3,5}$-3-alkyl enol ether (Alkyl enol ether) with a hydride abstractor and an alcohol selected from the group consisting of alcohols of the formula:

(a) R_{31}-OH, where R_{31} is as defined above,

(b) R_{32}-OH, where R_{32} is as defined above,

(c) HO-(CH_2)-$(CR_{33}R_{34})_{n1}$-(CH_2)-OH where n_1, R_{33} and R_{34} are as defined above,

(d) HO-CH_2-CH_2-OH, by (1) contacting the $\Delta^{3,5}$-3-enol ether (3-alkyl enol ether). Useful hydride abstractors include those selected from the group consisting of

DDQ,

p-chloranil,

o-chloranil,

Mn^{+3}, Mn^{+7}, Pb^{+4}, Pd^{+2}, Ru^{+8}, Cr^{+6},

o-iodoxybenzoic acid,

o-iodoxybenzoic acid complex with DMSO,

o-iodoxybenzoic acid complex with

4-methoxypyridine-N-oxide,

N-methylmorpholine-N-oxide,

trimethylamine-N-oxide,

iodic acid (HIO_3),

iodine pentoxide (I_2O_5),

ceric ammonium nitrate,

iodosobenzene,

iodobenzenebistrifluoroacetate,

iodobenzenediacetate,

tritylfluoroborate, and by electrochemical oxidation with a catalytic amount of a hydride abstractor. It is preferred that the hydride abstractor is *p*-chloranil or DDQ, more preferably DDQ. One equivalent of the hydride abstractor is required; more is not harmful, just wasteful. It is preferred that the alcohol is neopentylglycol also known as dimethylpropyleneglycol or 2,2-dimethyl-1,3-propanediol . The solvent needs to dissolve the 3-alkyl enol ether (3-alkyl enol ether) starting material. Suitable solvents include methylene chloride, acetonitrile, THF, and the alike. The reaction is operable in the temperature range of about –78° to about 40°, preferred is about –15°. The reaction is very rapid and is complete in a few minutes at –15°. The entire process is preferably performed under essentially anhydrous conditions. The term "hydride abstractor" as used herein means the reagent effects the net removal of one of the hydrogen atoms at C-7 of the 3-dienol ether, and does not imply any mechanism by which this removal occurs. It is preferred that the a $\Delta^{4,6}$-ketal (I-P) is selected from the group consisting of

17β-hydroxypregna-4,6,9(11)-trien-3-one-21-carboxylic acid, γ-lactone, cyclic 3-(2',2'-dimethyl-1',3'-propanediyl ketal),

17β-hydroxypregna-4,6,9(11)-trien-3-one-21-carboxylic acid, γ-lactone, cyclic 3-ethanediyl ketal.

CHART C discloses that the 7α-substituted steroid (II) can also be transformed to the corresponding *cis*-oxyenedione (X-*cis*) by (1) contacting the 7α-substituted steroid (II) with ozone in the presence of a C_1-C_4 alcohol and (2) contacting the mixture of step (1) with a hydroperoxy-deoxygenating agent. The preferences for $R_{7\text{-}1}$, X_1 R_b, R_c, R_d and the other variable substituents are as set forth above as previously stated. The 7α-substituted steroid (II) is dissolved in a suitable C_1-C_4 alcohol, or mixture thereof. It is preferred that the C_1-C_4 alcohol is a C_1 and C_3 alcohols; it is more preferred the alcohol is a C_1 alcohol. Cosolvents such as methylene chloride can also be used if necessary. The nature of the solvent/co-solvent is not critical as long as it will dissolve the reactants at the cold temperature at which the process is performed. The nature of the alcohol is not critical as it is eventually lost from the steroid molecule. The reaction temperatures can be as low as about –100° up to about 40°. It is preferred that the temperature be from about –78° to about –20°; it is more preferred that the temperature be about –50°. Ozone is passed thru the reaction mixture as is known to those skilled in the art until the process of step (1) is complete. The course of the reaction is monitored as is known those skilled in the art. When the reaction of step (1) is complete, the reaction mixture of step (1) is contacted with a hydroperoxy-deoxygenating agent. It is preferred that the hydroperoxy-deoxygenating agent is trimethylphosphite. It is realized that for other processes of this invention the preferred hydroperoxy-deoxygenating agent was dimethylsulfide, but here the preferred agent is trimethylphosphite. The reaction mixture is then slowly permitted to warm to 20-25°. The reaction will proceed rapidly when it reaches the correct temperature for the particular 7α-substituted steroid (II). The *cis*-oxyenedione (X-*cis*) product can be carried along without isolation and purification if desired.

CHART C further discloses that the *cis*-oxyenedione (X-*cis*) can be transformed to the corresponding *trans*-oxyenedione (X-*trans*). The process is performed in the same manner and same way that the *cis*-enedione (III-*cis*), of CHART A, was transformed to the corresponding *trans*-enedione (III-*trans*).

The *cis*-oxyenedione (X-*cis*) or the *trans*-oxyenedione (X-*trans*), or a mixture thereof, can be transformed to the corresponding hydroperoxy compound (IV-OOH),

and/or hydroxy compound (IV-OH), and/or biscarbonyl compound (V) and/or carboxylic acid (VI) or mixture thereof in the same manner and same way as the *cis*-enedione (III-*cis*) or the *trans*-enedione (III-*trans*), or a mixture thereof, was transformed to the corresponding hydroperoxy compound (IV-OOH), and/or hydroxy compound (IV-OH), and/or biscarbonyl compound (V) and/or carboxylic acid (X) or mixture thereof. The hydroperoxy compound (IV-OOH), and/or hydroxy compound (IV-OH), and/or biscarbonyl compound (V) and/or carboxylic acid (X) or mixture thereof are then transformed to eplerenone (IX) in the same manner and same was as previously discussed for the process of CHART A.

The *cis*-oxyenedione (X-*cis*) or the *trans*-oxyenedione (X-*trans*), or a mixture thereof, can be transformed to the corresponding carboxylic acid (VI) by reaction with an oxidatively cleaving agent in the same manner and same way as the hydroxy compound (IV-OH), and/or biscarbonyl compound (V) are transformed to the corresponding carboxylic acid (VI).

CHART D sets forth the preferred process of the invention (when R_{7-1} is –A1) with regard to the steroid A-/B-ring, that the steroid A-ring is not protected. However, given the different variable substituents of the steroid C- and D-rings and combinations of variable substituents possible, in some cases it may be preferred to protect the steroid A-ring as would be apparent to one skilled in the art. But in general, it is preferred that the steroid A-ring not be protected and the preferred process be that of CHART D.

CHART E sets forth the preferred process of the invention with the preferred variable substituents for each intermediate for the conversion of the $\Delta^{4,6}$-3-keto steroid (I) to eplerenone (IX).

CHART F discloses the reversible nature of the conversion of the carboxylic acid (VI) with the 5,7-lactone (VII).

CHART G discloses the general process of the invention when the adduct $-R_{7-1}$ is the cyclic adduct (-A2). The 7α-substituted steroid (II) is formed in the same manner as discussed above for CHART A when the adduct is (-A1). Then the 7α-substituted steroid (II) where R_{7-1} is (-A2) is reacted in the same way, with the same reagents as used in CHART A for (-A1) to give intermediates of the same type as the intermediates of CHART A for adduct (-A1). The processes of CHARTs A and G are

analogous, the reactants are the same and used in the same order. The intermediates produced are either isomers or homologs of each other.

CHART H discloses the general process of the invention when the adduct R_{7-1} is (-B), (-C), (-D1), (-D2) and (-D3). The process of CHART H is a two step process. The first step of the process is to transform the $\Delta^{4,6}$-3-keto steroid or ketal thereof (I) starting material to the corresponding 7α-substituted steroid (II) where R_{7-1} is a substituent selected from the group consisting of

$$-CR_{b2}{=}M \quad \text{(-B)}$$

$$-C{\equiv}C\text{-}R_{c2} \quad \text{(-C)}$$

$$-CH_2\text{-}CH{=}CH_2 \quad \text{(-D1)}$$

$$-CH{=}C{=}CH_2 \quad \text{(-D2)}$$

$$-CH_2\text{-}C{\equiv}C\text{-}H \quad \text{(-D3)}$$

The second step is oxidative cleavage of the 7α-substitutent to give a carboxylic acid functionality, -CO-OH of the carboxylic acid (VI). In the olefinic substituent (-B), "M" is a group which forms a double bond with carbon and is restricted to carbon, nitrogen and oxygen. The substituent R_{b2} is a group that can be transformed into a hydroxyl group by either oxidation or hydrolysis. With the acetylenic substituent (-C), the group R_{c2} can be virtually any group since it is ultimately lost when the triple bond is cleaved to a carboxylic acid (VI). Likewise with the three-carbon unsaturated substituents (-D1), (-D2) and (-D3), two of the three carbon atoms are cleaved oxidatively, leaving a carboxylic acid group. In transforming the $\Delta^{4,6}$-3-keto steroid or ketal thereof (I) starting material to the corresponding 7α-substituted steroid (II), the $\Delta^{4,6}$-3-keto steroid or ketal thereof (I) starting material is reacted with the nucleophile selected from the group consisting of

(d) of the formula (B)

$$R_a\text{-}CE_1{=}M \quad \text{(B)}$$

(e) of the formula (C)

$$R_a\text{-}C{\equiv}C\text{-}E_2 \quad \text{(C)}$$

(f) of the formulas (D1, D2 and D3)

$$R_a\text{-}CH_2\text{-}CH{=}CH_2 \quad \text{(D1)}$$

$$R_a\text{-}CH{=}C{=}CH_2 \quad \text{(D2)}$$

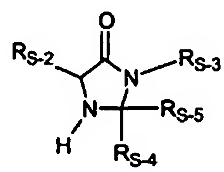
$$R_a\text{-}CH_2\text{-}C{\equiv}C\text{-}H \quad \text{(D3)}$$

where R_a, E_1, E_2, M are as defined above, in the presence of:

(1) a Lewis Acid,

(2) a proton acid with a pK_a of < about 5 or

(3) a salt of a secondary amine of the formula



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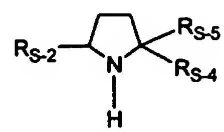


with an acid of pK_a of < about 2. The Lewis acid both accelerates the conjugate addition and favors formation of the 7α-stereochemistry.

Adducts (-B) and (-C) are transformed into –CO-OH of carboxylic acid (VI) by treatment with one or more oxidizing agents. The oxidizing agent(s) must be capable of cleaving the C=M double bond to a carbon-oxygen double bond, cleaving the C-R_{b2} single bond to a carbon-oxygen single bond, and cleaving the carbon-carbon triple bond to carboxylic acid. The choice of oxidizing agent(s) depends on the inherent difficulty of oxidation of the substituent -CR_{b2}=M or –C≡C-R_{c2}. The greater the difficulty of oxidation, the stronger the oxidizing agent that will be required. Suitable oxidizing agents include ozone, singlet oxygen, triplet oxygen, hydrogen peroxide, hydroperoxides, percarboxylic acids, hypohalites, and the like. In the case of 2-methylfuran adduct (II), transformation into carboxylic acid (VI) is preferably accomplished by treatment with potassium hypobromite followed by ozone followed by dimethylsulfide followed by hydrogen peroxide.

The allyl adduct (-D1) is transformed into –CO-OH of the carboxylic acid (VI) by double bond isomerization to –CH=CH-CH_3 followed by ozonization with an oxidative work-up (such as sodium chlorite). The double bond isomerization can be

accomplished by any of the following reagents, rhodium trichloride in ethanol at reflux, $HRuCl[P(-\varphi)_3]_3$ at about 90°, $LiNH(CH_2)_3NH_2$ (lithium 1,3-diaminopropane) at 20-25°, $PdCl_2(\varphi\text{-}CN)_2$ in toluene at about 80°, $HRh(CO)[P(-\varphi)_3]_3$ at 20-25°, $ClRh[P(-\varphi)_3]_3$ in toluene at reflux, $Cl_2Ru[P(-\varphi)_3]_3$ at 100° and cobalt chloride/sodium borohydride/$P(-\varphi)_3$ at about –18°.

The propargyl adduct (-D2) is transformed into the –CO-OH functionality of the carboxylic acid (VI) by base or transition metal-catalyzed isomerization to adduct (-C) when R_{c2} is C_1 alkyl, which is cleaved by the method discussed above. Suitable bases for isomerization of (-D2) to (-C) include sodium amide in ammonia or THF, potassium 3-aminopropylaminde (known as "KAPA") in THF, potassium hydroxide in ethylene glycol at about 150°, potassium *t*-butoxide in DMSO or *t*-butanol, or sodium or potassium hydride in DMF or THF. Suitable transition metal catalysts include $Yb[\varphi_2C{=}N\text{-}\varphi](HMPA)_4$ and $HCo(N_2)\,[P(-\varphi)_3]_3$.

The allenyl adduct (-D3) is transformed into the –CO-OH functionality of the carboxylic acid (VI) by ozonization with an oxidative work-up (such as sodium chlorite).

The present invention includes a four-step process for the transformation of a 7α-substituted steroid (II) to the corresponding carboxylic acid (VI) product. The four steps are (1) ring opening, (2) ozonolysis, (3) reaction with a hydroperoxy deoxygenating agent and (4) reaction with an oxidatively cleaving agent. The four-step process of the invention produces better yields of the carboxylic acid (VI) than expected based on prior art process steps. The carboxylic acid (VI) is obtained by:

(1) contacting the 7α-substituted steroid of formula (II) with an agent selected from the group consisting of:

(a) a halogenating agent in the presence of water and a base whose conjugate acid has a pK_a of > about 8,

(b) an oxygen donating agent,

(c) electrochemical oxidation,

(d) a quinone in the presence of water or

(e) nonquinone oxidants; and

(2) contacting the reaction mixture of step (1) with ozone in the presence of an alcohol of the formula $R_{7\text{-}2}$-OH;

(3) contacting the reaction mixture of step (2) with a hydroperoxy deoxygenating agent and

(4) contacting the reaction mixture of step (3) with an oxidatively cleaving agent. Each of these steps was thoroughly discussed above when the steps of the process were discussed individually. This process combines those same steps and they are practiced in the same manner and same way as discussed above.

The present invention includes a three-step process for the transformation of a 7α-substituted steroid (II) to the corresponding carboxylic acid (VI) product, see EXAMPLE 34, Step (1). The three steps are (1) ozonolysis, (2) reaction with a hydroperoxy deoxygenating agent and (3) reaction with an oxidatively cleaving agent. The three-step process of the invention is a process to prepare the carboxylic acid (VI) which comprises:

(1) contacting a 7α-substituted steroid (II) with ozone in the presence of an alcohol of the formula R_{7-2}-OH;

(2) contacting the reaction mixture of step (1) with a hydroperoxy deoxygenating agent and

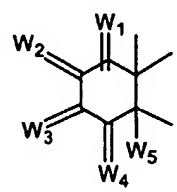
(3) contacting the reaction mixture of step (2) with an oxidatively cleaving agent. Each of these steps was thoroughly discussed above when the steps of the process were discussed individually. This process combines those same steps and they are practiced in the same manner and same way as discussed above. The carboxylic acid (VI) can be readily transformed to its tautomer-like the bislactone (VII) by contacting with an acid, see EXAMPLE 34, Step (2). In the process of the invention it is the carboxylic acid (VI) which is transformed to the methyl ester (VIII) and ultimately to eplerenone (IX). It is possible to isolate and purify this carboxylic acid (VI) by crystallization. However, one runs the risk that it will isomerize to the bislactone (VII) which is more thermodynamically stable. Therefore, as a practical matter it is preferable not to stop at the end of EXAMPLE 34, Step (1) but carry on thru the reaction mixture and isolate and crystallize the bislactone (VII). Hence, it is easier and preferable to carry the process exemplified in EXAMPLE 34 on thru Step (2), purify the bislactone (VII) obtained and then convert the bislactone (VII) back to the carboxylic acid (VI) for transformation to the methyl ester (VIII).

Eplerenone (IX) is a pharmaceutical agent useful for the treatment of hyperaldosteronism, edema, hypertension and congestive heart failure, see US Patent 4,559,332.

The present invention also includes a novel process to transform 11α-hydroxy steroids to the corresponding $\Delta^{9(11)}$-steroids. The $\Delta^{9(11)}$-functionality is very useful in producing eplerenone (IX) because it is readily transformed to the corresponding 9α,11α-epoxide functionality of eplerenone (IX).

The 11α-hydroxy steroid (CIV) starting materials are known to those skilled in the art. More particularly, the 11α-hydroxy-17-lactone (CI), 11α,17β-dihydroxypregn-4-en-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester, is known, see, *Drugs of the Future*, 24(5), 488-501 (1999), compound (VI).

For the 11α-hydroxy steroids (CIV) it is preferred that the steroid A-ring is:



(A-ring)

(1) W_1 is –H:-H and W_2 is –H:-H or W_1 is W_{1-1}:W_{1-2} and W_2 is W_{2-1}:W_{2-2} where one of W_{1-1} or W_{1-2} is taken together with one of W_{2-1} or W_{2-2} to form a second bond between the carbon atoms to which they are attached and the other or W_{1-1} or W_{1-2} and W_{2-1} or W_{2-2} is –H; W_3 is =O, W_4 is W_{4-1}:W_{4-2} where one of W_{4-1} and W_{4-2} is taken together with W_5 to form a second bond between the carbon atoms to which they are attached and the other of W_{4-1} and W_{4-2} is –H;

(2) W_3 is =O, W_4 is –H:-H and W_5 is in the α-orientation and is ⋯⋯O-CO- (attached at C_7 to form a 5,7-lactone) and where W_1 and W_2 are as defined above;

(3) W_3 is –O-W_{3-3}:-O-W_{3-4}; W_4 is W_{4-3}:W_{4-4}, where one of W_{4-3} and W_{4-4} is taken together with W_5 to form a second bond between the atoms to which they are attached and the other of W_{4-3} and W_{4-4} is –H; W_{3-3} and W_{3-4} are:

(a) the same or different and are C_1-C_5 alkyl,

(b) taken together to form a cyclic moiety selected from the group consisting of:

(i) –CH_2-CH_2-,

(ii) $-CH_2-CH_2-CH_2-$,

(iii) $-CH_2-C(CH_3)_2-CH_2-$; and where W_1 and W_2 are as defined above;

(4) W_3 is $-O-W_{3-3}$:$-O-W_{3-4}$; W_4 is $-H$:$-H$; W_5 forms a second bond between C_5 and C_6; W_{3-3} and W_{3-4} are as defined above:

(5) W_3 is W_{3-5}:W_{3-6}; where

(a) one of W_{3-5} and W_{3-6} is $-H$ and the other of W_{3-5} and W_{3-6} is:

(i) $-O-$ W_{3-5A} where W_{3-5A} is C_1-C_3 alkyl,

(ii) $-O-CO-W_{3-5A}$ where W_{3-5A} is as defined above,

(iii) $-N(W_{3-5A})_2$ where W_{3-5A} is as defined above,

(iv) piperazinyl,

(v) morpholinyl,

(vi) piperidinyl,

(b) W_{3-5} and W_{3-6} are taken together with the carbon atom to which they are attached to form a cyclic moiety including:

(i) $-O-CH_2-CH_2-O-$,

(ii) $-O-CH_2-CH_2-CH_2-O-$,

(iii) $-O-CH_2-C(CH_3)_2-CH_2-O-$ and where W_4 is $-H$:$-H$; W_5 forms a second bond between C_5 and C_6;

(6) W_3 is W_{3-7}:W_{3-8} and where W_4 is W_{4-7}:W_{4-8} where

(a) one of W_{3-7} and W_{3-8} is:

(i) $-O-$ W_{3-7A} where W_{3-7A} is C_1-C_3 alkyl,

(ii) $-O-CO-W_{3-7A}$ where W_{3-7A} is as defined above,

(iii) $-N(W_{3-7A})_2$ where W_{3-7A} is as defined above,

(iv) piperazinyl,

(v) morpholinyl,

(vi) piperidinyl, and where the other of W_{3-7} and W_{3-8} is taken together with one of W_{4-7} and W_{4-8} to form a second bond between the carbon atoms to which they are attached and the other of W_{4-7} and W_{4-8} is $-H$; W_5 forms a second bond between C_5 and C_6;

(7) W_3 is α-W_{3-9}:β-W_{3-10}; where W_{3-9} is $-H$ and W_{3-10} is:

(a) $-O-CO-W_{3-10A}$ where W_{3-10A} is C_1-C_3 alkyl,

(b) $-O-CO-O-W_{3-10B}$ where W_{3-10B} is

(i) C_1-C_4 alkyl,

(ii) $-\varphi$ optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy,

(iii) $-CH_2-\varphi$ where φ is optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy; where WR_4 is –H:-H; and W_5 forms a second bond between the carbon atoms at C_5 and C_6; and where W_1 and W_2 are as defined above;

(8) W_3 is α-W_{3-9}:β-W_{3-10}; where W_4 is W_{4-9}:W_{4-10} where W_{3-9} and W_{3-10} are as defined above; where one of W_{4-9} and W_{4-10} taken together with W_5 forms a second bond between the atoms to which they are attached and the other of W_{4-9} and W_{4-10} is –H; and where W_1 and W_2 are as defined above.

It is more preferred that the steroid A-ring functionality be:

(1) W_1 is –H:-H and W_2 is –H:-H or W_1 is W_{1-1}:W_{1-2} and W_2 is W_{2-1}:W_{2-2} where one of W_{1-1} or W_{1-2} is taken together with one of W_{2-1} or W_{2-2} to form a second bond between the carbon atoms to which they are attached and the other or W_{1-1} or W_{1-2} and W_{2-1} or W_{2-2} is –H; W_3 is =O, W_4 is W_{4-1}:W_{4-2} where one of W_{4-1} and W_{4-2} is taken together with W_5 to form a second bond between the carbon atoms to which they are attached and the other of W_{4-1} and W_{4-2} is –H;

(7) W_3 is α-W_{3-9}:β-W_{3-10}; where W_{3-9} is –H and W_{3-10} is:

(b) $-CO-W_{3-10A}$ where W_{3-10A} is C_1-C_3 alkyl,

(c) $-CO-O-W_{3-10B}$ where W_{3-10B} is

(i) C_1-C_4 alkyl,

(ii) $-\varphi$ optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy,

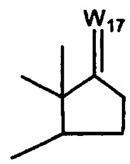
(iii) $-CH_2-\varphi$ where φ is optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy; where WR_4 is –H:-H; and W_5 forms a second bond between the carbon atoms at C_5 and C_6; and where W_1 and W_2 are as defined above.

It is even more preferred that the steroid A-ring functionality be:

(1) W_1 is –H:-H and W_2 is –H:-H or W_1 is W_{1-1}:W_{1-2} and W_2 is

W_{2-1}:W_{2-2} where one of W_{1-1} or W_{1-2} is taken together with one of W_{2-1} or W_{2-2} to form a second bond between the carbon atoms to which they are attached and the other or W_{1-1} or W_{1-2} and W_{2-1} or W_{2-2} is –H; W_3 is =O, W_4 is W_{4-1}:W_{4-2} where one of W_{4-1} and W_{4-2} is taken together with W_5 to form a second bond between the carbon atoms to which they are attached and the other of W_{4-1} and W_{4-2} is –H;

For the 11α-hydroxy steroids (CIV), it is preferred that the steroid D-ring is:



(D-ring)

where W_{17} is:

(1) =O,

(2) α-W_{17-1}:β-W_{17-2} where:

(a) W_{17-1} and W_{17-2} are taken together with the attached carbon atom to form an epoxide of the formula ····CH_2-O–,

(b) W_{17-1} and W_{17-2} are taken together with the attached carbon atom to form a lactone of the formula ····CH_2-CH_2-CO-O–;

(3) α-W_{17-3}:β-W_{17-4} where

(a) W_{17-3} is:

(i) –H,

(ii) –O-CO-W_{17-3A} where W_{17-3A} is –H or –CO-W_{17-3B} where W_{17-3B} is C_1-C_4 alkyl or –φ and

(b) W_{17-4} is –CO-CH_3;

(4) α-W_{17-5}:β-W_{17-6} where

(a) W_{17-5} is:

(i) –O-CO-W_{17-5A} where W_{17-5A} is C_1-C_4 alkyl or –φ,

(b) W_{17-6} is:

(i) –CO-CH_2-O-W_{17-6A} where W_{17-6A} is C_1-C_4 alkyl or –φ.

For the eplerenone-type compounds, it is preferred that W_{17} is:

(1) =O,

(2) α-W_{17-1}:β-W_{17-2} where:

(a) W_{17-1} and W_{17-2} are taken together with the attached carbon atom to form an epoxide of the formula ····CH_2-O–,

(b) W_{17-1} and W_{17-2} are taken together with the attached carbon atom to form a lactone of the formula ····CH_2-CH_2-CO-O–.

It is more preferred that for the eplerenone-type compounds that W_{17} is:

(1) =O,

(2) α-W_{17-1}:β-W_{17-2} where:

(b) W_{17-1} and W_{17-2} are taken together with the attached carbon atom to form a lactone of the formula ····CH_2-CH_2-CO-O–.

For the progesterones and hydroxyprotesterones it is preferred that that W_{17} is:

(3) α-W_{17-3}:β-W_{17-4} where

(a) W_{17-3} is:

(i) –H,

(ii) –O-CO-W_{17-3A} where W_{17-3A} is –H or –CO-W_{17-3B} where W_{17-3B} is C_1-C_4 alkyl or –φ and

(b) W_{17-4} is –CO-CH_3.

For the corticoids it is preferred that W_{17} is:

(4) α-W_{17-5}:β-W_{17-6} where

(a) W_{17-5} is:

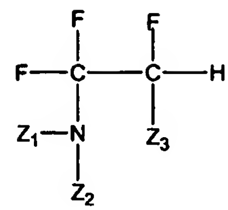
(i) –O-CO-W_{17-5A} where W_{17-5A} is C_1-C_4 alkyl or –φ,

(b) W_{17-6} is:

(i) –CO-CH_2-O-W_{17-6A} where W_{17-6A} is C_1-C_4 alkyl or –φ.

The preferred combinations of steroid A-, B- and D-rings, especially for the eplerenone-type compounds, includes the ring systems set forth in CHART C. The 11α-hydroxy steroids (CIV) of CHART C are known to those skilled in the art or can be readily prepared by known methods from known compounds.

In the process of the present invention the 11α-hydroxy-17-lactones (CI) or 11α-hydroxy steroids (CIV) starting material is contacted with a N-fluoroalkylamine reagent of the formula (CVI)



(CVI)

where:

Z_1 is C_1-C_4 alkyl;

Z_2 is C_1-C_4 alkyl and where Z_1 and Z_2 together with the attached nitrogen atom form a 5- or 6-member heterocycle selected from the group consisting of pyrrolidinyl, piperazinyl, piperidinyl and morpholinyl;

Z_3 is –F or –CF_3. It is preferred that Z_1 and Z_2 are C_1-C_3 alkyl. It is more preferred that Z_1 and Z_2 are C_1 alkyl or C_2 alkyl. It is preferred that the N-fluoroalkylamine (CVI) is N-(1,1,2,3,3,3-hexafluoropropyl)diethylamine, which is known as Ishikawa reagent, or 1,1,2,2-tetrafluoroethyl-N,N-dimethylamine.

The process of the invention is preferably performed by use of about 1 equivalent of 11α-hydroxy-17-lactone (CI) or 11α-hydroxy steroid (CIV) and from about 1 to about 1.5 equivalents of Ishikawa reagent; more preferred is about 1.2 equivalents of Ishikawa reagent. It is preferable to perform the process of the invention in a temperature range of from about 20 to about 82°; more preferably from about 40 to about 70°. The reaction usually takes from about 1 hr to about 24 to complete depending on reaction conditions especially temperature and concentration. For example at about 60° and 0.8 molar, the reaction takes about 3 hours.

The 11α-hydroxy-17-lactone (CI) or11α-hydroxy steroid (CIV) can be added to the N-fluoroalkylamine reagent (CVI) or the N-fluoroalkylamine reagent (CVI) can be added to the 11α-hydroxy-17-lactone (CI) or11α-hydroxy steroid (CIV); it is more practical to add the N-fluoroalkylamine reagent (CVI) to the 11α-hydroxy-17-lactone (CI) or11α-hydroxy steroid (CIV).

It is preferred to perform the process of the present invention in a solvent that is dry (KF is < 0.5%), such as acetonitrile.

The $\Delta^{9(11)}$-17-lactone of formula (CII), 17β-hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester, is known, see US Patent 4,559,332, Example 1(d) and International Publication WO98/25948, page 284. It is

useful in the preparation of a pharmaceutical agent, 9α,11α-epoxy-17β-hydroxypregn-4-en-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester, known as eplerenone (CIII).

The steroid C-ring functionality $\Delta^{9(11)}$- of compounds (CII) and (CV) is a very useful functionality to chemists skilled in the art of steroids. It can be readily transformed to the corresponding 9α,11α-epoxy functionality and the 9α-fluoro-11β-hydroxy functionality as well as 11-keto and others as is well known to those skilled in the art. These compounds are useful pharmaceutical agents. Hence, the process of the invention as it pertains to the transformation of the 11α-hydroxy steroid (CIV) to the corresponding $\Delta^{9(11)}$- steroid (CV) is a very useful process and is operable with a wide variety of 11α-hydroxy steroids (CIV) as is apparent to those skilled in the art. This includes progesterones, 17α-hydroxyprogesterones, corticoids as well as the usual common derivatives and analogs thereof such as esters, etc. Therefore, the process produces $\Delta^{9(11)}$-steroids (CV) which are useful intermediates in the preparation of pharmaceutically useful steroids. One skilled in the art with a given $\Delta^{9(11)}$-steroid (CV) would know how to transform it to a pharmaceutically useful product.

The present invention also includes a number of processes for transforming 11α-hydroxy compounds to the corresponding $\Delta^{9(11)}$-compounds by one or more processes described above. For example, described are processes for the transformation of (1) a 11α-hydroxy-7α-substituted steroid (II) to the corresponding $\Delta^{9(11)}$- 7α-substituted steroid (II), (2) a process for transforming a 11α-hydroxy *cis* enedione (III-*cis*) or 11α-hydroxy *trans* enedione (III-*trans*) to the corresponding $\Delta^{9(11)}$-*trans* enedione (III-*trans*) and (3) for transforming a 11α-hydroxy-hydroxy compound (IV-OH) or a 11α-hydroxy-hydroperoxy compound (IV-OOH) or a 11α-hydroxy biscarbonyl compound (V) or mixture thereof to the corresponding $\Delta^{9(11)}$-carboxylic acid (VI).

DEFINITIONS AND CONVENTIONS

The definitions and explanations below are for the terms as used throughout this entire document including both the specification and the claims.

I. CONVENTIONS FOR FORMULAS AND DEFINITIONS OF VARIABLES

The chemical formulas representing various compounds or molecular fragments in the specification and claims may contain variable substituents in addition to expressly defined structural features. These variable substituents are identified by a letter or a letter followed by a numerical subscript, for example, "Z_1" or "R_i" where "i" is an integer. These variable substituents are either monovalent or bivalent, that is, they represent a group attached to the formula by one or two chemical bonds. For example, a group Z_1 would represent a bivalent variable if attached to the formula CH_3-C(=Z_1)H. Groups R_i and R_j would represent monovalent variable substituents if attached to the formula CH_3-CH_2-C(R_i)(R_j)H_2. When chemical formulas are drawn in a linear fashion, such as those above, variable substituents contained in parentheses are bonded to the atom immediately to the left of the variable substituent enclosed in parenthesis. When two or more consecutive variable substituents are enclosed in parentheses, each of the consecutive variable substituents is bonded to the immediately preceding atom to the left which is not enclosed in parentheses. Thus, in the formula above, both R_i and R_j are bonded to the preceding carbon atom. Also, for any molecule with an established system of carbon atom numbering, such as steroids, these carbon atoms are designated as C_i, where "i" is the integer corresponding to the carbon atom number. For example, C_6 represents the 6 position or carbon atom number in the steroid nucleus as traditionally designated by those skilled in the art of steroid chemistry. Likewise the term "R_6" represents a variable substituent (either monovalent or bivalent) at the C_6 position.

Chemical formulas or portions thereof drawn in a linear fashion represent atoms in a linear chain. The symbol "-" in general represents a bond between two atoms in the chain. Thus CH_3-0-CH_2-CH(R_i)-CH_3 represents a 2-substituted-1-methoxypropane compound. In a similar fashion, the symbol "=" represents a double bond, e.g., CH_2=C(R_i)-O-CH_3, and the symbol "≡" represents a triple bond, e.g., HC≡C-CH(R_i)-CH_2-CH_3. Carbonyl groups are represented in either one of two ways: -CO- or -C(=O)-, with the former being preferred for simplicity.

Chemical formulas of cyclic (ring) compounds or molecular fragments can be represented in a linear fashion. Thus, the compound 4-chloro-2-methylpyridine can be represented in linear fashion by N^*=C(CH_3)-CH=CCl-CH=C^*H with the convention that the atoms marked with an asterisk (*) are bonded to each other resulting in the

formation of a ring. Likewise, the cyclic molecular fragment, 4-(ethyl)-1-piperazinyl can be represented by $-N^{*}-(CH_2)_2-N(C_2H_5)-CH_2-C^{*}H_2$.

A rigid cyclic (ring) structure for any compounds herein defines an orientation with respect to the plane of the ring for substituents attached to each carbon atom of the rigid cyclic compound. For saturated compounds which have two substituents attached to a carbon atom which is part of a cyclic system, $-C(X_1)(X_2)-$ the two substituents may be in either an axial or equatorial position relative to the ring and may change between axial/equatorial. However, the position of the two substituents relative to the ring and each other remains fixed. While either substituent at times may lie in the plane of the ring (equatorial) rather than above or below the plane (axial), one substituent is always above the other. In chemical structural formulas depicting such compounds, a substituent (X_1) which is "below" another substituent (X_2) will be identified as being in the alpha (α) configuration and is identified by a broken, dashed or dotted line attachment to the carbon atom, i.e., by the symbol "- - -" or "...". The corresponding substituent attached "above" (X_2) the other (X_1) is identified as being in the beta (ß) configuration and is indicated by an unbroken line attachment to the carbon atom.

When a variable substituent is bivalent, the valences may be taken together or separately or both in the definition of the variable. For example, a variable R_i attached to a carbon atom as $-C(=R_i)-$ might be bivalent and be defined as oxo or keto (thus forming a carbonyl group (-CO-) or as two separately attached monovalent variable substituents α-R_{i-j} and ß-R_{i-k}. When a bivalent variable, R_i, is defined to consist of two monovalent variable substituents, the convention used to define the bivalent variable is of the form "α-R_{i-j}:ß-R_{i-k}" or some variant thereof. In such a case both α-R_{i-j} and ß-R_{i-k} are attached to the carbon atom to give $-C(\alpha$-$R_{i-j})$(ß-$R_{i-k})-$. For example, when the bivalent variable R_6, $-C(=R_6)-$ is defined to consist of two monovalent variable substituents, the two monovalent variable substituents are α-R_{6-1}:ß-R_{6-2}, ... α-R_{6-9}:ß-R_{6-10}, etc, giving $-C(\alpha$-$R_{6-1})$(ß-$R_{6-2})-$, ... $-C(\alpha$-$R_{6-9})$(ß-$R_{6-10})-$, etc. Likewise, for the bivalent variable R_{11}, $-C(=R_{11})-$, two monovalent variable substituents are α-R_{11-1}:ß-R_{11-2}. For a ring substituent for which separate α and ß orientations do not exist (e.g. due to the presence of a carbon carbon double bond in the ring), and for a

substituent bonded to a carbon atom which is not part of a ring the above convention is still used, but the α and ß designations are omitted.

Just as a bivalent variable may be defined as two separate monovalent variable substituents, two separate monovalent variable substituents may be defined to be taken together to form a bivalent variable. For example, in the formula $-C_1(R_i)H-C_2(R_j)H-$ (C_1 and C_2 define arbitrarily a first and second carbon atom, respectively) R_i and R_j may be defined to be taken together to form (1) a second bond between C_1 and C_2 or (2) a bivalent group such as oxa (-O-) and the formula thereby describes an epoxide. When R_i and R_j are taken together to form a more complex entity, such as the group -X-Y-, then the orientation of the entity is such that C_1 in the above formula is bonded to X and C_2 is bonded to Y. Thus, by convention the designation "... R_i and R_j are taken together to form $-CH_2-CH_2-O-CO-$ ..." means a lactone in which the carbonyl is bonded to C_2. However, when designated "... R_j and R_i are taken together to form $-CO-O-CH_2-CH_2-$the convention means a lactone in which the carbonyl is bonded to C_1.

The carbon atom content of variable substituents is indicated in one of two ways. The first method uses a prefix to the entire name of the variable such as "C_1-C_4", where both "1" and "4" are integers representing the minimum and maximum number of carbon atoms in the variable. The prefix is separated from the variable by a space. For example, "C_1-C_4 alkyl" represents alkyl of 1 through 4 carbon atoms, (including isomeric forms thereof unless an express indication to the contrary is given). Whenever this single prefix is given, the prefix indicates the entire carbon atom content of the variable being defined. Thus C_2-C_4 alkoxycarbonyl describes a group $CH_3-(CH_2)_n-0-CO-$ where n is zero, one or two. By the second method the carbon atom content of only each portion of the definition is indicated separately by enclosing the "C_i-C_j" designation in parentheses and placing it immediately (no intervening space) before the portion of the definition being defined. By this optional convention (C_1-C_3)alkoxycarbonyl has the same meaning as C_2-C_4 alkoxycarbonyl because the "C_1-C_3" refers only to the carbon atom content of the alkoxy group. Similarly while both C_2-C_6 alkoxyalkyl and (C_1-C_3)alkoxy(C_1-C_3)alkyl define alkoxyalkyl groups containing from 2 to 6 carbon atoms, the two definitions differ since the former definition allows either the alkoxy or alkyl portion alone to contain 4

or 5 carbon atoms while the latter definition limits either of these groups to 3 carbon atoms.

When the claims contain a fairly complex (cyclic) substituent, at the end of the phrase naming/designating that particular substituent will be a notation in (parentheses) which will correspond to the same name/designation in one of the CHARTS which will also set forth the chemical structural formula of that particular substituent.

II. DEFINITIONS

All temperatures are in degrees Celsius.

TLC refers to thin-layer chromatography.

LC refers to liquid chromatography.

ESTDLC refers to external standard liquid chromatography.

THF refers to tetrahydrofuran.

DMAP refers to *p*-dimethylaminopyridine.

DDQ refers to 2,3-dichloro-5,6-dicyano-1,4-benzoquinone.

DBU refers to 1,8-diazabicyclo[5.4.0]undec-7-ene.

DBN refers to 1,5-diazabicyclo[4.3.0]non-5-ene.

DABCO refers 1,4-diazabicyclo[2.2.2]octane.

Chromatography (column and flash chromatography) refers to purification/separation of compounds expressed as (support, eluent). It is understood that the appropriate fractions are pooled and concentrated to give the desired compound(s).

Carboxylic acid (VI) refers to and includes the pharmaceutically acceptable salts thereof.

CMR refers to C-13 magnetic resonance spectroscopy, chemical shifts are reported in ppm (δ) downfield from TMS.

NMR refers to nuclear (proton) magnetic resonance spectroscopy, chemical shifts are reported in ppm (d) downfield from TMS.

In the present invention the terms conversion/transformation or convert/transform are used interchangeable and mean the same thing, the reaction of one compound to form a different compound by the process described.

TMS refers to trimethylsilyl.

Oxone refers to $KHSO_5$.

-ϕ refers to phenyl (C_6H_5).

MS refers to mass spectrometry expressed as m/e, m/z or mass/charge unit. $[M + H]^+$ refers to the positive ion of a parent plus a hydrogen atom. EI refers to electron impact. CI refers to chemical ionization. FAB refers to fast atom bombardment.

Pharmaceutically acceptable refers to those properties and/or substances which are acceptable to the patient from a pharmacological/toxicological point of view and to the manufacturing pharmaceutical chemist from a physical/chemical point of view regarding composition, formulation, stability, patient acceptance and bioavailability.

When solvent pairs are used, the ratios of solvents used are volume/volume (v/v).

When the solubility of a solid in a solvent is used the ratio of the solid to the solvent is weight/volume (wt/v).

Δ^9-Canrenone refers to 17β-hydroxypregna-4,6,9-trien-3-one-21-carboxylic acid, γ-lactone.

Eplerenone refers to 9α,11α-epoxy-17β-hydroxypregn-4-en-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester.

Neopentylglycol refers to $HO\text{-}CH_2\text{-}C(CH_3)_2\text{-}CH_2\text{-}OH$.

Iodosobenzene refers to φI=O.

Iodobenzenebistrifluoroacetate refers to $\varphi I(O\text{-}CO\text{-}CF_3)_2$.

Iodobenzenediacetate refers to $\varphi I(O\text{-}CO\text{-}CH_3)_2$.

Tritylfluoroborate is also known as triphenylcarbenium fluoroborate and refers to $\varphi_3C^+BF_4^-$.

acac refers to acetylacetonate.

dppb refers to diphenylphosphino butane.

Tf refers to trifluoromethanesulfonate.

Dimethylsulfide refers to CH_3SCH_3.

Ishikawa reagent refers to N-(1,1,2,2,3,3,3)hexafluoropropyldiethylamine.

An "oxidatively cleaving agent" is a reagent that oxidizes the biscarbonyl compound (V) or hydroxy compound (IV-OH) to the carboxylic acid (VI).

A "hydroperoxy-deoxygenating agent" is a reagent that removes an oxygen

atom from a hydroperoxide compound (IV-OOH) to give the corresponding hydroxy compound (IV-OH).

A "deoxygenating agent" is a reagent that removes one oxygen atom from a molecule. The "hydroperoxy-deoxygenating agent" is thus a particular type of deoxygenating agent.

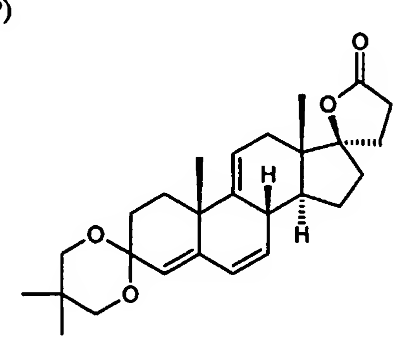
A "carboxylic acid forming agent" is a reagent that induces a hydroperoxide compound (IV-OOH) to rearrange to a carboxylic acid (VI).

An "oxygen donating agent" is a reagent that provides an oxygen atom to a 7α-substituted steroid (II) to transform it into a cis enedione (III-*cis*).

EXAMPLES

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, practice the present invention to its fullest extent. The following detailed examples describe how to prepare the various compounds and/or perform the various processes of the invention and are to be construed as merely illustrative, and not limitations of the preceding disclosure in any way whatsoever. Those skilled in the art will promptly recognize appropriate variations from the procedures both as to reactants and as to reaction conditions and techniques.

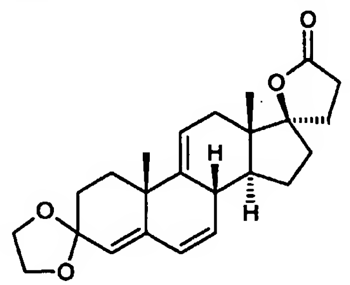
EXAMPLE 1 17β-Hydroxypregna-4,6,9(11)-trien-3-one-21-carboxylic acid, γ-lactone, cyclic 3-(2',2'-dimethyl-1',3'-propanediyl ketal) (I-P)



17β-hydroxypregna-4,6,9(11)-trien-3-one-21-carboxylic acid, γ-lactone 3-methyl enol ether (I, 3.00 g, 8.4629 mmoles) and lithium perchlorate (199.6 mg, 1.8761 mmoles, 0.22 equivalents) are slurried in acetonitrile (20 ml) and methylene chloride (10) are cooled to –15°, treated with 2,2-dimethyl-1,3-propyleneglycol (2.19 g, 21.027 mmoles, 2.48 equivalents), then treated drop wise over 73 min. with a solution of DDQ (2.29 g, 10.088 mmoles, 1.19 equivalents) in ethyl acetate. After

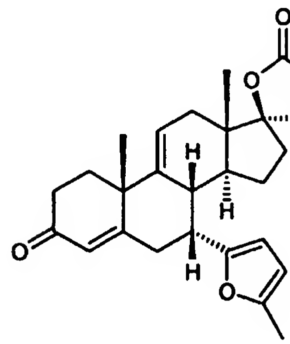
stirring for 40 min, the reaction mixture is quenched with ammonium hydroxide (28%, 5 ml), diluted with ethyl acetate, concentrated, diluted with methylene chloride, and filtered. The filtrate is diluted with ethyl acetate, washed with aqueous sodium bicarbonate/sodium chloride followed by water, then filtered through magnesol, eluting with methylene chloride. The eluate is concentrated to give solids which are triturated with toluene, dried by a stream of nitrogen to give the title compound, CMR ($CDCl_3$) 14.44, 22.53, 22.78, 23.02, 24.89, 28.85, 29.22, 30.07, 30.18, 31.31,32.92, 35.37, 38.56, 39.03, 44.35, 44.43, 70.54, 70.65, 95.17, 95.43, 116.80, 120.23, 127.82, 130.27, 141.83, 145.08 and 176.61 δ; NMR ($CDCl_3$) 0.95, 0.97, 1.03, 1.18, 1.3-2.8, 3.5-3.7, 5.44, 5.71, 5.80 and 6.02 δ.

EXAMPLE 2 17β-Hydroxypregna-4,6,9(11)-trien-3-one-21-carboxylic acid, γ-lactone, cyclic 3-ethanediyl ketal (I-P)



17β-hydroxypregna-4,6,9(11)-trien-3-one-21-carboxylic acid, γ-lactone 3-methyl enol ether (I, 300 mg, 0.8463 mmoles) in methylene chloride (5 ml) is cooled to –15° then treated with ethylene glycol (220 mg, 3.544 mmoles, 4.19 equivalents). To this mixture is added drop wise over 30 min. a solution of DDQ (230 mg, 1.0132 mmoles, 1.20 equivalents). After the addition is complete, the reaction is stirred at –15° for 5 min., at which time TLC analysis (ethyl acetate/cyclohexane, 66/34) shows conversion of the starting methyl enol ether (R_f = 0.69) into the corresponding ethylene ketal (R_f = 0.54) was nearly complete. The reaction is then quenched with concentrated ammonium hydroxide (0.5 ml), and filtered. The filtrate is then filtered through 1.0 g cartridge grade magnesol and concentrated to give the title compound, by comparison with an authentic sample, CMR ($CDCl_3$) 14.37, 22.95, 24.54, 29.15, 30.28, 31.23, 32.87, 35.30, 38.17, 38.45, 44.27, 44.37, 64.15, 64.70, 95.07, 105.94, 116.85, 122.39, 127.41, 130.24, 141.71, 145.76 and 176.51 δ; NMR ($CDCl_3$) 0.97, 1.18, 1.3-2.9, 3.8-4.1, 5.29, 5.45, 5.70 and 5.99 δ.

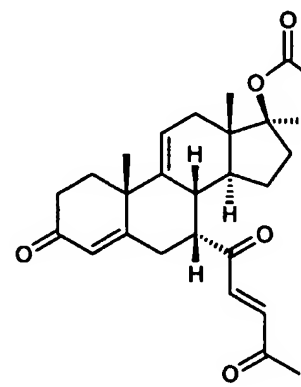
EXAMPLE 3 17β-Hydroxy-7α-(5'-methyl-2'-furyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (II)



Δ^9-canrenone (I, 90.0 g, 0.2659 moles) is mixed with nitromethane (730-735 ml). Then 2-methylfuran (49.5 ml, 45.04 g, 0.5487 moles, 2.06 equivalents) is added. The resulting mixture is cooled to −20° then treated with absolute ethanol (15.8 ml, 12.55 g, 0.2723 moles, 1.02 equivalents) followed by boron trifluoride etherate, (d = 1.120; 37.2 ml, 41.66 g, 0.2936 moles, 1.10 equivalents). The mixture is recooled to −18.4° and stirred for 17 hrs., at which time the reaction was complete by LC. The reaction mixture is quenched with ammonia (15% aqueous, 225 ml). The mixture is warmed to above 0°, water (200 ml) is added, the organic phase is separated, and the aqueous phase is extracted with methylene chloride (2 x 200 ml). The organic extracts are dried over magnesium sulfate (100 g) then filtered through magnesol (100 g cartridge grade), washing the cake with methylene chloride (5 x 200 ml). The eluate is then concentrated under reduced pressure to a foam, slurried with ethyl acetate (200 ml) and reconcentrated, then dissolved in ethyl acetate (950 ml) at 50° to 60°. The mixture is concentrated to about 500 ml volume, then diluted with cyclohexane (250 ml). The product begins to crystallize slowly. The slurry is reconcentrated to about 500 ml volume, cooled to 20-25°, further concentrated to about 400 ml volume, then cooled to 0°. After overnight at 0°, the slurry is filtered and the cake washed with cyclohexane followed by heptane and dried in a vacuum oven at 50° to give the title compound, TLC = 0.37 (ethyl acetate/cyclohexane, 66/34), CMR ($CDCl_3$) 13.38, 14.12, 23.18, 26.83, 29.14, 31.26, 32.93, 33.93, 34.18, 35.39, 37.57, 38.52, 40.78, 41.90, 42.39, 44.08, 95.19, 105.89, 107.12, 119.73, 126.24, 149.99, 152.74, 167.45, 76.53 and 198.56; NMR ($CDCl_3$) 0.95, 1.43, 1.4-2.6, 2.16, 2.93, 3.30, 5.68 and 5.74 δ.

The filtrate is concentrated to a foam which is dissolved in ethyl acetate (40 ml), concentrated to about 20 ml, seeded, diluted with cyclohexane (20 ml), concentrated to about 30 ml, cooled to 0° over the weekend, then filtered, washed with ethyl acetate/cyclohexane (1/2) and dried to give additional title compound.

EXAMPLE 4 17β-Hydroxy-7α-(*trans*-1',4'-dioxopent-2'-en-1'yl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (III-*trans*)



Step A: 17β-Hydroxy-7α-(*cis*-1',4'-dioxopent-2'-en-1'yl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (III-*cis*)

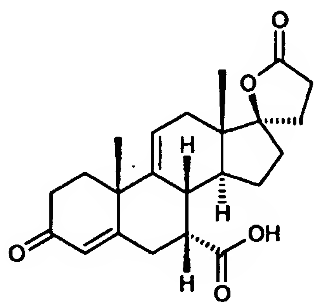
A mixture of 17β-hydroxy-7α-(5'-methyl-2'-furyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (II, EXAMPLE 3, 5.04 g, 11.9843 mmoles) and potassium acetate (1.7 g, 17.32 mmoles, 1.45 equivalents) in THF (40 ml) and water (12.5 ml) at 23.8° is treated with dibromantin (2.0 g, 6.995 mmoles, 0.58 equivalents) followed by isobutyl vinyl ether (500 μl, 384 mg, 3.834 mmoles, 0.32 equivalents). The reaction mixture is stirred at 20-25° for 1 hr., at which time conversion of the starting material (II, $R_f = 0.50$) into cis- and trans-enedione ($R_f = 0.11$) is complete by TLC (ethyl acetate/cyclohexane, 66/34). The reaction mixture is diluted with water (200 ml) and extracted with methylene chloride (2 x 100 ml). The extracts are combined, washed with water (50 ml), dried over magnesium sulfate, filtered and concentrated to give the *cis*-enedione (III-*cis*).

Step B: 17β-Hydroxy-7α-(*trans*-1',4'-dioxopent-2'-en-1'yl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (III-*trans*)

The concentrate (Step A) is taken up in chloroform (100 ml) and the mixture is stirred at 20-25° for 20 hrs., at which time conversion of *cis*-enedione into *trans*-

enedione is judged to be complete as measured by TLC and LC (*cis/trans* = 1.1/98.9). The mixture is then concentrated and the concentrate is taken up in ethyl acetate (20 ml) at 20-25° and diluted with cyclohexane (80 ml), which induces crystallization. The slurry is cooled, filtered, and the cake washed with cyclohexane and dried under reduced pressure at 50° to give the title compound, CMR ($CDCl_3$) 13.98, 23.28, 27.08, 28.66, 29.01, 31.26, 32.77, 33.61, 34.01, 35.22, 35.28, 40.48, 40.51, 42.41, 44.43, 48.13, 94.77, 118.81, 126.03, 135.89, 137.04, 142.16, 165.21, 176.32, 197.81, 198.26 and 200.18; NMR ($CDCl_3$) 1.04, 1.30, 1.51, 1.5-3.6, 2.45, 5.71, 5.78 and 6.89 δ; MS (electrospray) m/e = 435 (p^+-1) negative ion mode;

EXAMPLE 5 17β-Hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone (VI)



Step A: 17β-hydroxy-7α-(1'-oxo-2'-isopropoxy-2'-hydroxy-ethyl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (IV-OH); 17β-hydroxy-7α-(1'-oxo-2'-isopropoxy-2'-hydrohydroperoxyethyl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (IV-OOH) and 17β-hydroxy-7α-(2'-oxo-acetyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (V)

A mixture of 17β-hydroxy-7α-(*trans*-1',4'-dioxo-pent-2'-en-1'yl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (III-trans, EXAMPLE 4, 551.8 mg, 1.2640 mmoles) in isopropanol (11 ml) and methylene chloride (5 ml) is cooled to −55°. Ozone in oxygen is bubbled through this mixture until 0.4 area% (by LC) *trans*-enedione (III) remained. The mixture is purged of ozone by sparging with nitrogen for 7 minutes to give a mixture of the title compounds.

Step B: 17β-hydroxy-7α-(1'-oxo-2'-isopropoxy-2'-hydroxy-ethyl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (IV-OH), 17β-

hydroxy-7α-(1',2'-dioxo-ethyl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (V) and 17β-Hydroxy-7α-(2'-oxo-acetyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (V)

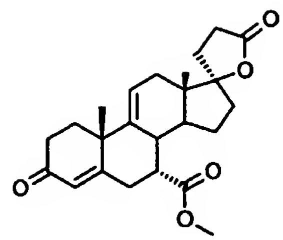
The mixture of Step A is then quenched with dimethylsulfide (340 μl, 288 mg, 4.630 mmoles, 3.66 equivalents), warmed to 20-25°, stirred at 20-25° for 50 min. to give a mixture of the title compounds.

Step C: 17β-Hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone (VI)

The mixture of Step B is then treated with hydrogen peroxide (70% aqueous, 430 μl, 560 mg, containing 392 mg (11.52 mmoles, 9.12 equivalents) of hydrogen peroxide) and a solution of potassium bicarbonate (637.7 mg, 6.369 mmoles, 5.04 equivalents) in water (8 ml). The resulting two-phase mixture is diluted with enough methanol to produce a one-phase mixture (5 ml), which is then stirred at 20-25° for 16 hrs., then diluted to a volume of 500 ml with methanol for purpose of LC analysis. LC analysis indicates the title compound is obtained by comparison with a known compound.

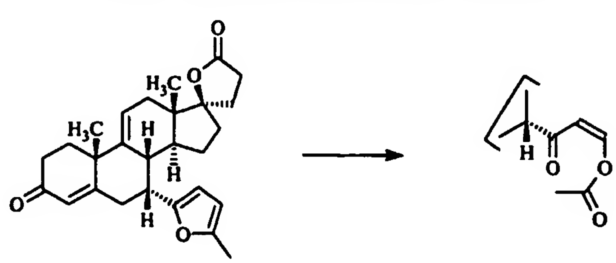
A 20.0 ml portion of the 500 ml solution was withdrawn and further diluted with methanol to a volume of 50 ml. This solution (containing 17.3 mg [0.0450 mmoles] carboxylic acid by LC) is concentrated to a low volume, diluted with water, acidified with hydrochloric acid (1N), and extracted with methylene chloride (2 x). The two extracts are each washed in sequence with water, then combined and concentrated. The concentrate is taken up in methanol/toluene (1/1; 2 ml) and treated with a mixture of trimethylsilyldiazomethane, $(CH_3)_3SiCHN_2$, in hexane (2.0 M, 0.25 ml, 0.50 mmoles, 11.1 equivalents). TLC analysis (ethyl acetate/cyclohexane; 66/34) indicates the title compound is obtained, $R_f = 0.23$; LC analysis (210 nm detection) indicates the same retention time as a known standard and that the title compound is obtained.

EXAMPLE 6 17β-Hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester (VIII)



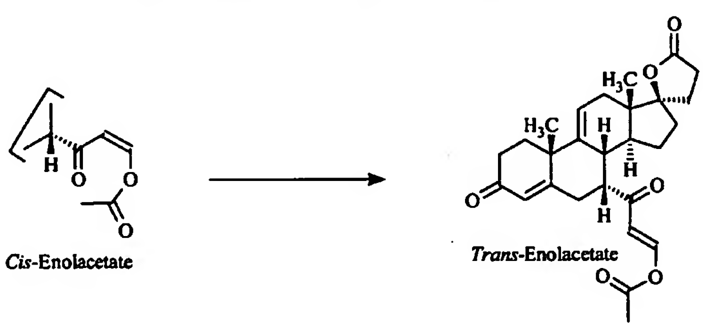
The remainder of the 500 ml mixture of Step C of EXAMPLE 5 (479 ml, containing 414.4 mg [1.0777 mmoles] 17β-hydroxypregna-4,9(11)-dien-3-one 7α,21-dicarboxylic acid, γ-lactone (VI, EXAMPLE 5C) is concentrated partially, diluted with water (20 ml), concentrated to a volume of about 20 ml, treated with hydrochloric acid (18 ml) and extracted with methylene chloride (25 ml, then 2 x 15 ml). The extracts are washed with water (30 ml), combined, and concentrated to a volume of 50.0 ml. Half of this mixture is concentrated to a low volume, diluted with ethyl acetate, and extracted with potassium bicarbonate (25% aqueous, 20 ml, then 10 ml). The extracts are combined, acidified to pH 3 with hydrochloric acid (1N) and extracted with methylene chloride (40 ml, then 2 x 15 ml). The extracts are then combined, washed with water, concentrated to a volume of <1 ml, and treated with a solution of sodium carbonate (349.6 mg, 3.298 mmoles, 6.12 equivalents based on carboxylic acid) in water (1.0 ml) followed by tetra-*n*-butylammonium bisulfate, (n-butyl)$_4$NHSO$_4$, (20.4 mg, 0.0601 mmoles, 0.11 equivalents) followed by dimethylsulfate (108 μl, 144.0 mg, 1.14 mmoles, 2.11 equivalents). The mixture is diluted with methylene chloride (0.1 ml), stirred at 20-25° for 11.5 hrs., treated with hydrochloric acid (1 N, 10 ml) and extracted with methylene chloride (10 ml, then 2 x 5 ml). The extracts are combined, washed with water, and concentrated to give the title compound, consistent with a known standard.

EXAMPLE 7 17β-Hydroxy-7α-(*cis*-3'-acetoxyacryloyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (X-*cis*)



A stream of O_3/O_2 (ozone/oxygen) is passed through a cold (-78°) mixture of 17β-hydroxy-7α-(5'-methyl-2'-furyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (II, EXAMPLE 3, 3.0138 g, 7.1663 mmoles) in methylene chloride (40 ml) and methanol (10 ml) until the starting material had been consumed (LC, 25 min),then the mixture is purged with O_2 followed by nitrogen, quenched with trimethylphosphite (3.0 ml, 3.16 g, 25.435 mmoles, 3.55 equivalents), and warmed to 20-25°. After stirring for 1 hr., LC analysis indicates the title compound is obtained, CMR (100 MHz, $CDCl_3$) 198.49, 198.23, 176.43, 166.63, 166.10, 142.74, 142.44, 125.87, 118.12, 110.39, 94.99, 49.30, 44.47, 42.30, 40.59, ~40, 35.46, 35.33, 34.11, 33.63, 32.83, 31.37, 29.11, 27.26, 23.31, 20.67 and 14.06 δ; NMR (400 MHz, $CDCl_3$) 0.94, 1.40, 1.5-2.9, 2.29, 5.38, 5.63 and 7.48 δ.

EXAMPLE 8 17β-Hydroxy-7α-(*trans*-3'-acetoxyacryloyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (X-*trans*)

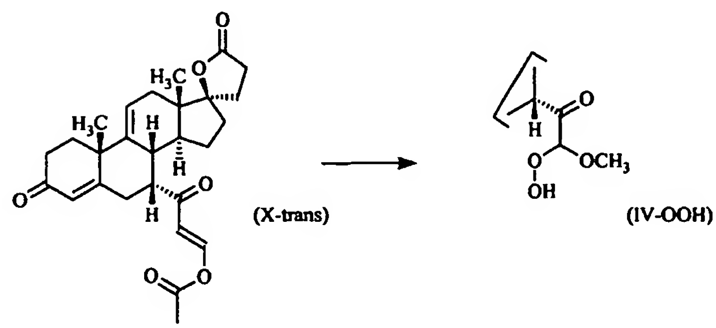


Cis-Enolacetate

Trans-Enolacetate

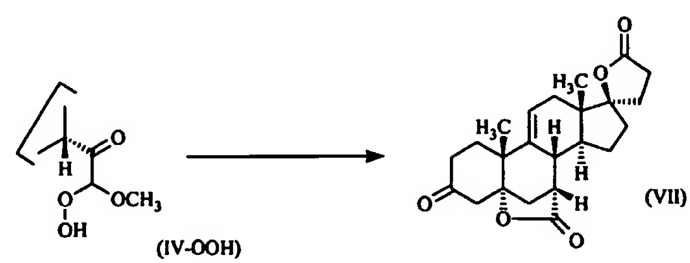
After stirring the reaction mixture of EXAMPLE 7, 17β-hydroxy-7α-(*cis*-3'-acetoxyacryloyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (X-*cis*, EXAMPLE 7) for 1 hr., the reaction mixture is quenched with hydrochloric acid (5% aqueous, 25 ml) and stirred at 20-25° for 20 min., at which time isomerization to *trans* is complete. The organic phase is then separated, concentrated, and flash chromatographed (silica gel, 150 g; gradient elution, 40% → 70% ethyl acetate/cyclohexane) to give the title compound. This material is then crystallized from ethyl acetate/heptane (70/30) to give the title compound in pure form, CMR (100 MHz, $CDCl_3$) 199.25, 198.39, 176.41, 166.79, 166.39, 149.00, 142.57, 125.67, 118.20, 113.11, 94.90, 47.75, 44.40, 42.40, 40.45, ~40, 35.63, 35.25, 34.01, 33.56, 32.73, 31.29, 29.04, 27.14, 23.32, 20.47 and 13.98 δ; NMR (400 MHz, $CDCl_3$) 1.14, 1.4-4.1, 1.61, 2.44, 5.75, 6.14 and 8.41 δ.

EXAMPLE 9 17β-Hydroxy-7α-(2'-hydroperoxy-2'-methoxyacetyl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (IV-OOH)



A stream of ozone/oxygen is passed through a cooled (-78°) mixture of 17β-hydroxy-7α-(*trans*-3'-acetoxyacryloyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (X-*trans*, EXAMPLE 8, 311.0 mg, 0.6872 mmoles) in methylene/methanol (2/1, 6 ml) until a blue color persisted (3 min.). The excess ozone is purged with oxygen followed by nitrogen, then the reaction mixture is warmed to 20-25° and diluted with methylene chloride to 10 ml. A portion of this mixture (3.5 ml, from 0.2405 mmoles *trans*-enolacetate) is concentrated to dryness to give the title compound.

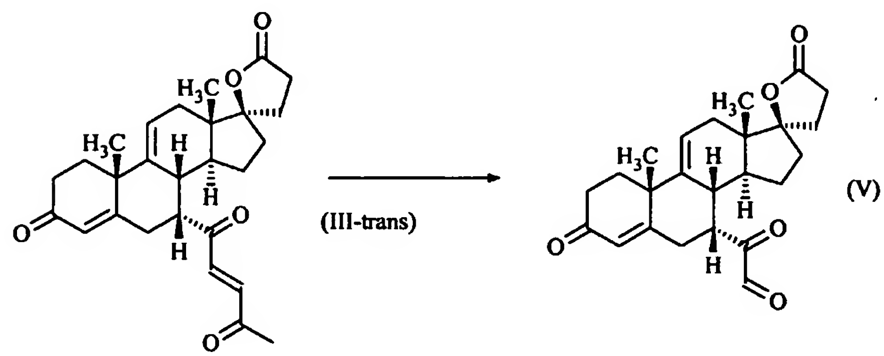
EXAMPLE 10 5α,17β-Dihydroxypregn-9(11)-ene-3-one 7α, 21-dicarboxylic acid, bis-γ-lactone (VII)



17β-Hydroxy-7α-(2'-hydroperoxy-2'-methoxyacetyl)pregna-4,9(11)-dien-3-one-21carboxylic acid, γ-lactone (IV-OOH, EXAMPLE 9, 3.5 ml, from 0.2405 mmoles *trans*-enolacetate) is concentrated to dryness and the residue dissolved in trifluoroacetic acid (1.0 ml), stirred at 20-25° for 20 min., then diluted with ethyl acetate (1.0 ml), washed with aqueous sodium bicarbonate, diluted with methylene

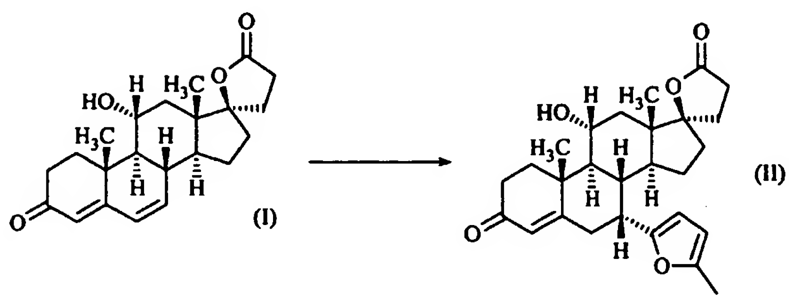
chloride (2.0 ml), washed with diluted aqueous hydrochloric acid and concentrated. The concentrate is taken up in methylene chloride (1.0 ml), stirred with aqueous hydrochloric acid (6N) for 30 min, then concentrated to give the title compound, CMR (100 MHz, $CDCl_3$) 206.39, 176.80, 175.59, 139.66, 124.11, 95.12, 91.11, 47.14, 43.99, 42.45, 41.66, 41.63, 41.15, 39.01, 37.04, 35.23, 33.08, 32.50, 31.42, 29.21, 23.16, 23.06 and 14.30 δ; NMR (400 MHz, $CDCl_3$) 0.94, 1.40, 1.5 – 2.6, 2.80, 5.70 δ; MS (CI, NH_3) m/e = 402 (100%, P + NH_4).

EXAMPLE 11 17β-Hydroxy-7α-(2'-oxo-acetyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (V)



A stream of ozone/oxygen is passed through a cooled (-79°) mixture of 17β-hydroxy-7α-(*trans*-1',4'-dioxopent-2'-en-1'yl)pregna-4,9-dien-3-one-21-carboxylic acid, γ-lactone (III-*trans*, EXAMPLE 4B, 503.4 mg, 1.1531 mmoles) in methylene chloride/methanol (1/1, 4.0 ml) until TLC analysis (acetone/methylene chloride, 3/7) indicates that conversion of starting material (R_f = 0.70) to a more polar product (R_f = 0.45) is complete (10 min.). The reaction mixture is then quenched with dimethylsulfide (0.20 ml, 169 mg, 2.72 mmoles, 2.34 equivalents), stirred at 20-25° for 1 hr., and then concentrated. The concentrate is flash chromatographed (silica gel, 60 g; gradient elution, acetone/methylene chloride 5% → 25%) to give the title compound, CMR (100 MHz, CD_3CN) 198.68, 197.54, 187.93, 176.09, 166.40, 142.33, 125.02, 118.56, 94.44, ~44, 42.49, 40.34, ~40, 39.87, 34.60, 33.83, 33.56, 33.32, 32.39, 30.53, 28.39, 26.16, 22.43 and 13.22 δ; NMR (400 MHz, CD_3CN) 0.87, 1.37, 1.2-2.9, 5.49, 5.63 and 8.93 δ; MS (CI, NH_3) m/e = 397 (P + H, 100%).

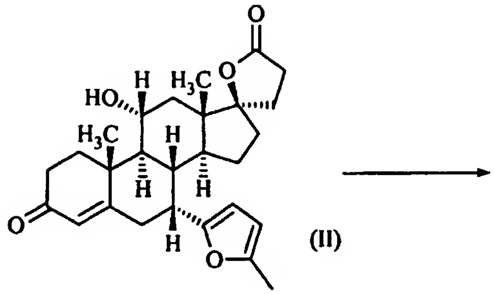
EXAMPLE 12 11α,17β-Dihydroxy-7α-(5'-methyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone (II)



A mixture of 11α-hydroxycanrenone (I, 30.00 g, 84.1586 mmoles) in nitromethane (240 ml) and methylene chloride (60 ml) is cooled to –20° then treated with 2-methylfuran (15.6 ml, 14.20 g, 0.1729 moles, 2.05 equivalents) followed by ethanol (5.1 ml, 4.03 g, 87.454 mmoles, 1.04 equivalents) followed by boron trifluoride diethyl etherate ($BF_3 \cdot OEt_2$, 12.0 ml, 13.44 g, 94.695 mmoles, 1.13 equivalents). The reaction mixture is stirred at –17° for 20 hrs., then quenched with ammonia (15% aqueous, 60 ml), extracted with methylene chloride (120 ml), dried over sodium sulfate (40 g) and concentrated. The concentrate is dissolved in methylene chloride/ethyl acetate (1/1, 300 ml) concentrated to a volume of 75 ml, diluted with 150 ml cyclohexane, concentrated to a volume of 200 ml, and filtered to give the title compound, CMR (75 MHz, $CDCl_3$) 199.59, 176.67, 170.11, 152.92, 150.28, 126.20, 108.67, 105.90, 95.18, 68.55, 52.05, 45.84, 45.58, 43.08, 39.73, 38.62, 38.42, 37.47, 36.54, 35.26, 34.17, 30.91, 29.05, 22.62, 18.40, 15.58 and 13.44 δ; NMR (300 MHz, $CDCl_3$) 1.01, 1.1-3.2, 1.41, 2.20, 4.12, 5.73, 5.83 and 5.93 δ.

The filtrate is concentrated. The concentrate is taken up in ethyl acetate (30 ml warm), cooled to 10°, and filtered to give a second crop of crystal of the title compound.

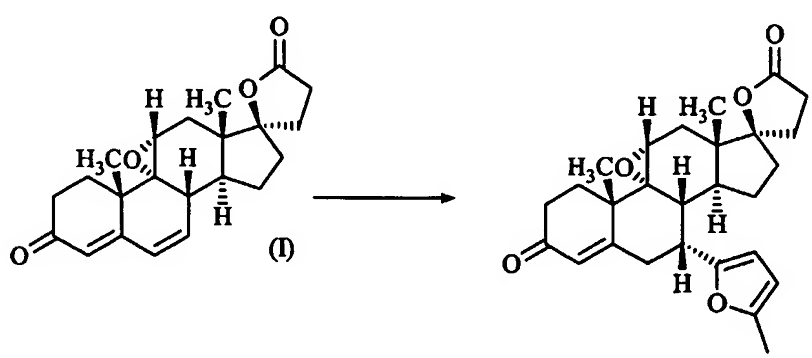
EXAMPLE 13 17β-Hydroxy-7α-(5'-methyl-2'-furyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (II)



(II) (II)

A mixture of 11α,17β-dihydroxy-7α-(5'-methyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone (II, EXAMPLE 12, 438.3 mg, 0.9994 mmoles) in THF (7.3 ml) is cooled to –50°, then treated all at once with solid phosphorous pentachloride, (PCl_5, 287.5 mg, 1.381 mmoles, 1.38 equivalents). After stirring for 42 min., analysis by LC indicates that conversion to the title compound is complete. After another 21 min., the mixture is quenched with water (22 ml) and warmed to 20-25°. After 20 min., the mixture is extracted with methylene chloride (2 x 15 ml), dried over magnesium sulfate, and concentrated to give the title compound, identified by LC retention time comparison with a sample from EXAMPLE 3.

EXAMPLE 14 9α,11α-Epoxy-17β-hydroxy-7α-(5'-methyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone (II)

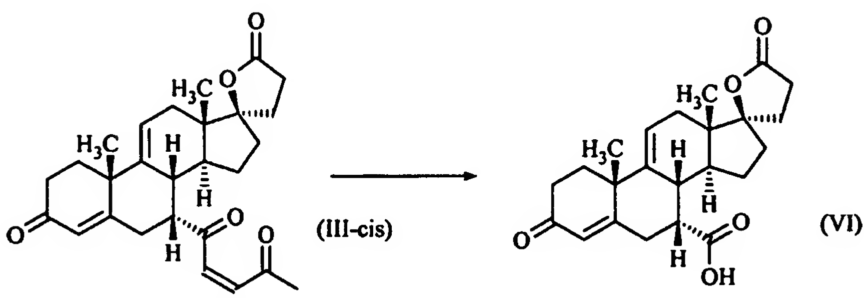


(I) (II)

A mixture of 9α,11α-epoxycanrenone (I, *J. Med. Chem.*, 6, 732 (1963) and *Helv. Chim. Acta* 80, 566 (1997), 10.0135 g, 28.2508 mmoles) in nitromethane (80 ml) and methylene chloride (20 ml) is cooled to –20° then treated with 2-methylfuran (5.10 ml, 4.64 g, 56.529 mmoles, 2.00 equivalents) followed by ethanol (1.7 ml, 1.343 g, 29.151 mmoles, 1.03 equivalents) followed by boron trifluoride diethyl etherate

($BF_3{\cdot}OEt_2$, 3.6 ml, 4.03 g, 28.408 mmoles, 1.01 equivalents). The reaction mixture is stirred at –20° for 24 hrs., at which time conversion to the product is complete as determined by LC, so the reaction is quenched with aqueous ammonia (15%, 10 ml), extracted with methylene chloride (2 x 100 ml), and concentrated to a residue which is flash chromatographed (560 g silica gel; gradient elution, 50% → 90% ethyl acetate/cyclohexane). The material obtained by chromatography is triturated with cyclohexane (100 ml) at reflux for two hrs., then cooled to 0° and filtered to give the title compound, CMR (75 MHz, $CDCl_3$) 198.10, 176.26, 165.67, 153.19, 149.96, 127.56, 107.92, 106.14, 94.66, 65.45, 49.92, 43.82, 40.00, 39.18, 37.43, 37.37, 35.54, 35.00, 33.24, 31.00, 30.81, 28.91, 26.98, 22.26, 22.00, 16.61 and 13.47 δ; NMR (300 MHz, $CDCl_3$) 1.02, 1.3-3.0, 1.52, 2.20, 3.28, 5.85, 5.92 and 6.01 δ. The assigned structure is confirmed by X-ray crystallography.

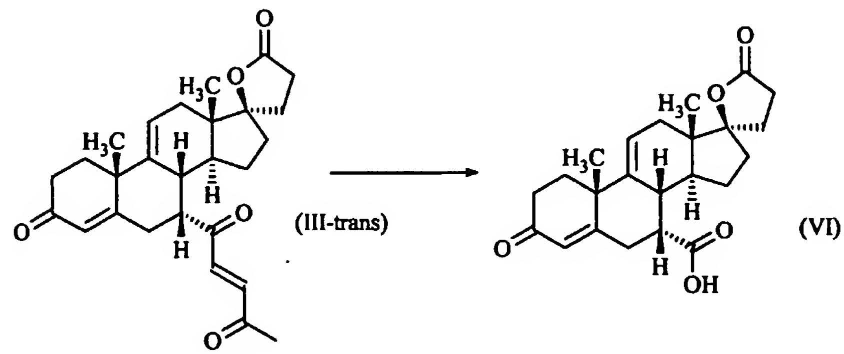
EXAMPLE 15 17β-Hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone (VI) via direct ozonization of 17β-hydroxy-7α-(*cis*-4'-oxo-pent-2'-enoyl)-3-oxo-pregna-4,9(11)-diene-21-carboxylic acid, γ-lactone (III-*cis*)



A stream of ozone/oxygen is passed through a cooled (-55°) mixture of 17β-hydroxy-7α-(*cis*-4'-oxo-pent-2'-enoyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (III-*cis*, EXAMPLE 4 Step A, 52.4 mg, 0.1200 mmoles) in methylene chloride/isopropyl alcohol (1/1, 3.0 ml) containing water (50 mg, 2.77 mmoles, 23.1 equivalents) until disappearance of starting material is complete by LC (126 secs.). The reaction mixture is then quenched with dimethylsulfide (0.033 ml, 27.9 mg, 0.449 mmoles, 3.74 equivalents), stirred at 20-25° for 45 min., then diluted with methanol (5 ml),treated with aqueous hydrogen peroxide (70%, 50 μl, containing 45.6 mg [1.34 mmoles, 11.2 equivalents] of hydrogen peroxide, treated with a mixture of potassium

bicarbonate (62.4 mg, 0.623 mmoles, 5.19 equivalents) in water (2 ml) and the resulting mixture stirred at 20-25°. After 15 hrs, analysis by LC indicates formation of the title compound.

EXAMPLE 16 17β-Hydroxypregna-4,9(11)-dien-3-one-7α, 21-dicarboxylic acid, γ-lactone (VI) via direct ozonization of 17β-hydroxy-7α-(*trans*-4'-oxo-pent-2'-enoyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (III-*trans*)

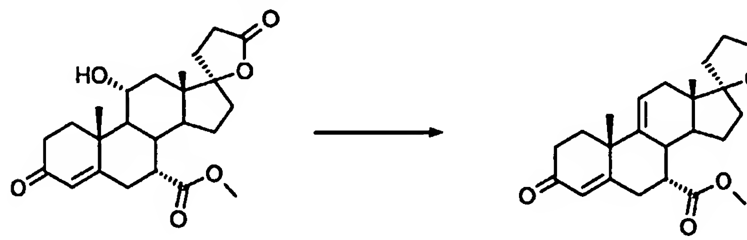


A stream of ozone/oxygen is passed through a cooled (-55°) mixture of 17β-hydroxy-7α-(*trans*-4'-oxo-pent-2'-enoyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (III-*trans*, EXAMPLE 4 Step B, 103.5 mg, 0.2371 mmoles) in methylene chloride/isopropyl alcohol (1/1, 3 ml) containing water (50 mg, 2.77 mmoles, 11.7 equivalents) until disappearance of starting material is complete by LC (100 secs.). The reaction mixture is then quenched with dimethylsulfide (CH_3SCH_3, 65 μl, 55.0 mg, 0.885 mmoles, 3.73 equivalents), stirred at 20-25° for 45 min., then diluted to a volume of 10.0 ml with methanol. A 5.0 ml portion of this mixture is treated with aqueous hydrogen peroxide (70%, 50 μl, containing 45.6 mg [1.34 mmoles, 11.3 equivalents] of hydrogen peroxide, treated with a mixture of potassium bicarbonate (59 mg, 0.589 mmoles, 4.97 equivalents) in water (2.1 ml), and the resulting mixture stirred at 20-25°. After 15 hrs., analysis by LC (ESTD) indicates formation of the title compound, CMR (100 MHz, $CDCl_3$) 199.96, 177.42, 174.28, 169.06, 142.10, 124.86, 118.60, 95.60, 44.23, 43.48,42.61, 40.38, 39.79, 35.59, 35.08, 33.73, 33.30, 32.57, 31.05, 28.98, 26.80, 22.92 and 13.68 δ; NMR (400 MHz, $CDCl_3$) 0.96, 1.42, 1.5-3.0, 4.28, 5.64 and 5.74 δ; MS (CI, NH_3; m/e) = 402 (P $+NH_4^+$).

EXAMPLE 17 5α,17β-Dihydroxypregn-9(11)-ene-3-one 7α, 21-dicarboxylic acid, bis-γ-lactone, 3-dimethyl ketal (VII-ketal)

5α,17β-Dihydroxypregn-9(11)-ene-3-one 7α, 21-dicarboxylic acid, bis-γ-lactone (VII, EXAMPLE 10) is treated with at least one equivalent of trimethyl ortho formate in the presence of a catalytic amount of *p*-toluenesulfonic acid by the procedure of International Publication WO98/25948, to give the title compound.

EXAMPLE 18 17β-hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester (VIII)



(VIII)

11α,17β-dihydroxypregn-4-en-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester (VIII, *Drugs of the Future*, 24(5), 488-501 (1999), compound (VI)), 5.00g, 12.0 mmol) is mixed with acetonitrile (15ml). N-(1,1,2,3,3,3)hexafluoropropyl)-diethylamine (V, 2.55 ml, 14.4 mmol) is added to this the steroid mixture and heated to 60° for 2.5 hours. The resulting mixture is cooled to 20-25° and the reaction is quenched with methanol (100 μL). A saturated aqueous solution of potassium bicarbonate (15 ml) is added. The acetonitrile is then removed under reduced pressure. The resulting mixture is extracted with methylene chloride (3 x 10 ml). The combined organic phases are washed with a aqueous solution of sodium chloride (10%, 20 ml). The solvent is dried with magnesium sulfate. The solvent is exchanged from methylene chloride to methyl *t*-butyl ether (MTBE). The mixture is concentrated to a final volume of 25 ml. The resulting slurry is stirred overnight and the final product, the title compound, is collected by filtration.

EXAMPLE 19 17β-hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester (VIII)

11α,17β-dihydroxypregn-4-en-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester (VIII, 5.00 g, 12.0 mmol) is placed in a flask with acetonitrile (15ml). To this mixture N-(1,1,2,3,3,3)hexafluoropropyl)- diethylamine (2.55 ml, 14.4 mmol) is

added and heated to 60° for 2 hrs. The mixture is cooled to 20-25° and the reaction is quenched with aqueous potassium bicarbonate (20% solution, 18 ml). The acetonitrile is removed under reduced pressure, the aqueous layer is extracted with methylene chloride (3 x 5 ml). The combined organic phases are washed with sodium chloride solution (10%, 10ml). The solvent is exchanged from methylene chloride to methyl isobutyl ketone/heptane to crystallize the title compound, mp = 198.6-199.5°; MS (m/z) calculated for $C_{24}H_{30}O_5$ = 398.5 (M+), found 398.9(M+); NMR ($CDCl_3$) 5.69, 5.64, 3.62, 2.97, 2.84-1.47, 1.38 and 0.93 δ; CMR ($CDCl_3$) 98.5, 176.4, 172.5, 166.5, 142.3, 125.6, 118.9, 95.0, 51.3, 43.0, 40.3, 35.6, 35.2, 34.1, 33.7, 32.8, 31.2, 29.0, 27.1, 23.2 and 14.0 δ.

EXAMPLE 20 17β-hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester (VIII)

11α,17β-dihydroxypregn-4-en-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester (VIII, 80.00 g, 192.1mmol) is placed in a flask with acetonitrile (80ml). To this mixture N-(1,1,2,3,3,3)hexafluoropropyl)- diethylamine (40.8 ml, 224.8 mmol) is added and heated slowly to 45 to 50°, then held for 1-2 hours. The mixture is cooled to 20-25° and the reaction is quenched with aqueous potassium bicarbonate (72 g in 288 ml). Methylene chloride (240 ml) is added and after mixing the layers are separated. The aqueous phase is extracted with methylene chloride (100ml). The combined organic phases are washed with water (240 ml). The solvent is exchanged from methylene chloride to methyl *tert*-butyl ether, and branched octane is added drop wise to crystallize the product which is the title compound.

EXAMPLE 21 17β-Hydroxy-7α-(5'-methyl-2'-furyl)-pregna-4,9-dien-3-one-21-carboxylic acid, γ-lactone (II)

Following the general procedure of EXAMPLE 3, using the same reactants and making non-critical variations, the title compound is obtained, CMR (100 MHz, $CDCl_3$) 198.56, 176.53, 167.45, 152.74, 149.99, 142.84, 126.24, 119.73, 107.12, 105.89, 95.19, 44.08, 42.39, 41.90, 40.78, 38.52, 37.57, 35.39, 34.18, 33.93, 32.93, 31.26, 29.14, 26.83, 23.18, 14.12 and 13.38 δ; NMR (400 MHz, $CDCl_3$) 0.95, 1.43, 1.4-2.6, 2.16, 2.93 and 5.7 δ.

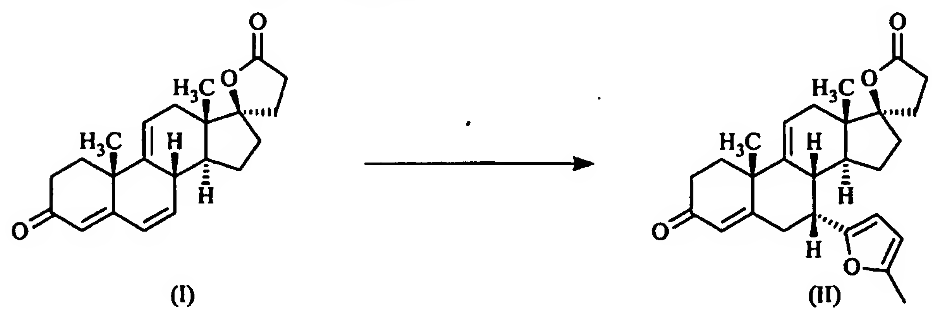
EXAMPLE 22 17β-Hydroxy-7α-(*cis*-1',4'-dioxopent-2'-en-1'yl)pregna-4,9-dien-3-one-21-carboxylic acid, γ-lactone (III-*cis*)

Following the general procedure of EXAMPLE 4, Step A, using the same reactants and making non-critical variations, the title compound is obtained, CMR (100 MHz, $CDCl_3$) 202.28, ~200, 199.05, 177.19, 166.56, 142.34, 138.49, 134.39, 126.37, 119.90, 95.57, 49.63, 44.90, 42.39, 41.08, 41.04, 35.82, 35.75, 34.49, 34.07, 33.25, 31.71, 30.12, 29.64, 27.49, 23.76 and 14.34 δ; NMR (400 MHz, $CDCl_3$) 0.93, 1.40, 1.4-2.9, 2.24, 5.66, 5.72, 6.15 and 6.28 δ.

EXAMPLE 23 17β-Hydroxy-7α-(2'-hydroperoxy-2'-methoxyacetyl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (IV-OOH)

Following the general procedure of EXAMPLE 9, using the same reactants and making non-critical variations, the title compound is obtained, CMR (100 MHz, $CDCl_3$) 203.54, 199.91, 177.51, 168.98, 142.42, 125.05, 117.89, 105.90, 95.58, 55.82, 44.21, 44.21, 42.17, 41.21, 40.37, 35.33, 34.84, 33.62, 33.16, 32.38, 30.79, 28.84, 26.72, 23.02 and 13.55 δ; NMR (400 MHz, $CDCl_3$) 0.94, 1.42, 1.4-2.8, 3.57, 4.34, 4.75 and 5.63 δ.

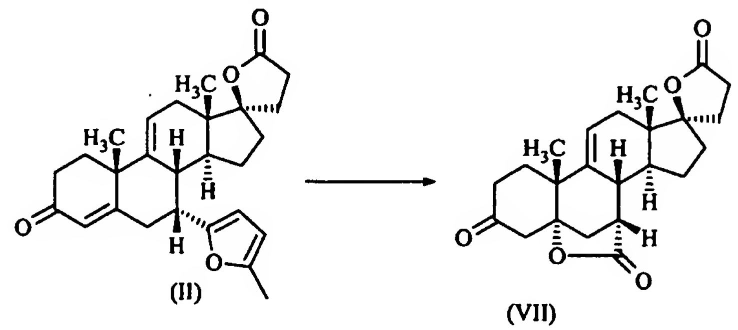
EXAMPLE 24 17β-Hydroxy-7α-(5'-methyl-2'-furyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (II)



A mixture of Δ^9-canrenone (I, 105 g, 0.31024 moles) in acetonitrile (450 ml) is treated with ethanol (21.0 g, 0.4558 moles, 1.47 equivalents), isopropanol (1.5 ml, 1.177 g, 19.592 mmoles, 0.063 equivalents), and 2-methylfuran (48.5 g, 0.5907 moles, 1.90 equivalents), then cooled to −18° and treated with boron trifluoride diethyl etherate (63.0 g, 0.4439 moles, 1.43 equivalents) over 4 hours. After stirring at −18° for 24 hrs., the mixture is quenched with triethylamine (38.0 g, 0.3755 moles, 1.21 equivalents) and concentrated to a thick slurry, which is diluted with water (350 ml), extracted with methylene chloride (400 ml), washed with water (350 ml), then concentrated, n-propyl acetate added, and further concentrated to give a slurry, which

is cooled to 0°, filtered, and the cake washed with *n*-propyl acetate/methyl-t-butyl ether (1/1) followed by methyl-*t*-butyl ether to give the title compound, identified by LC retention time comparison with a sample from EXAMPLE 3.

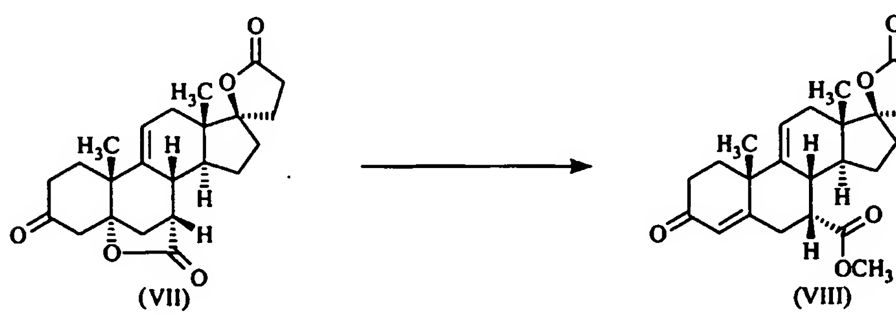
EXAMPLE 25 5α,17β-Dihydroxypregn-9(11)-ene-3-one, 7α,21-dicarboxylic acid, bis-γ-lactone (VII)



A mixture of 17β-hydroxy-7α-(5'-methyl-2'-furyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (II, EXAMPLE 24, 100 g, 0.23778 moles) and potassium acetate (50.0 g, 0.5094 moles, 2.14 equivalents) in acetone (500 ml) and water (150 ml) is cooled to –10° and treated with a slurry of dibromantin (34.0 g, 0.1189 moles, 0.50 molar equivalents) in water (100 ml) until a rise in the redox potential occurred. At this point, LC analysis indicated complete conversion into enedione (III-*cis*). The reaction mixture containing the enedione (III-*cis*) is then quenched with isobutyl vinyl ether (1.0 ml, 0.768 g, 7.668 mmoles, 0.032 equivalents), concentrated to a thick slurry, diluted with methylene chloride (200 ml), and treated with 20° concentrated hydrochloric acid (50.0 ml, 0.50 moles, 2.10 equivalents). The mixture is stirred at 20-25° for 2 hrs., at which time LC analysis indicated complete conversion to enedione (III-trans). The organic phase containing the enedione (III-*trans*) is separated, diluted with methylene chloride (80 ml) and methanol (300 ml), and cooled to –48°. A stream of O_3/O_2 is bubbled through this mixture until LC analysis indicated complete disappearance of the enedione (III-*trans*), then the mixture is quenched with dimethylsulfide (30.0 ml, 25.38 g, 0.4085 moles, 1.72 equivalents), stirred at –20° for 16 hrs., concentrated to a volume of about 300 ml, diluted with methanol (350 ml), concentrated to a volume of about 300 ml, diluted with isopropanol (40 ml) and methanol (80 ml), then treated with a warm (55-

60°) solution of potassium bicarbonate (120 g, 1.1986 moles, 5.04 equivalents) in water (240 ml). This slurry is cooled to 5-10°, then hydrogen peroxide (50%, 66.0 g, containing 33.0 g (0.9703 moles, 4.08 equivalents) hydrogen peroxide) is added over 3 hrs. The mixture is stirred for four hrs. and quenched with dimethylsulfide (40 ml, 33.84 g, 0.5447 moles, 2.29 equivalents). After stirring at 20-25° for 23 hrs., the mixture is diluted with methylene chloride (100 ml) and water (80 ml), and acidified to pH = 3.0 with concentrated hydrochloric acid. The two-phase mixture is heated to 36°, then the phases are separated and the aqueous phase extracted with methylene chloride (100 ml). The organic phases are combined, washed with water (75 ml), and the aqueous phase is back-extracted with methylene chloride (25 ml). The organic phases are combined, concentrated to a volume of 150 ml, then treated with benzenesulfonic acid (1.0 g of 90% pure material, containing 0.90 g (5.690 mmoles, 0.0239 equivalents) benzenesulfonic acid) and acetone (50 ml). The mixture is then concentrated atmospherically to a volume of 160 ml, then diluted with acetone (250 ml), concentrated to a volume of 200 ml, cooled to 12°, and filtered. The filter cake is washed with cold acetone (2 x 25 ml) and dried by nitrogen stream to give the title compound, CMR (100 MHz, $CDCl_3$) 206.08, 176.47, 175.41, 139.63, 124.00, 94.89, 90.97, 47.08, 43.90, 42.36, 41.58, 41.07, 38.93, 36.97, 35.16, 33.01, 32.42, 32.42, 31.35, 29.10, 23.08, 22.98 and 14.23 δ; NMR (400 MHz, $CDCl_3$) 0.94, 1.40, 1.4-2.8 and 5.70; MS (CI, NH_3) m/e = 385 (P + H, 100%).

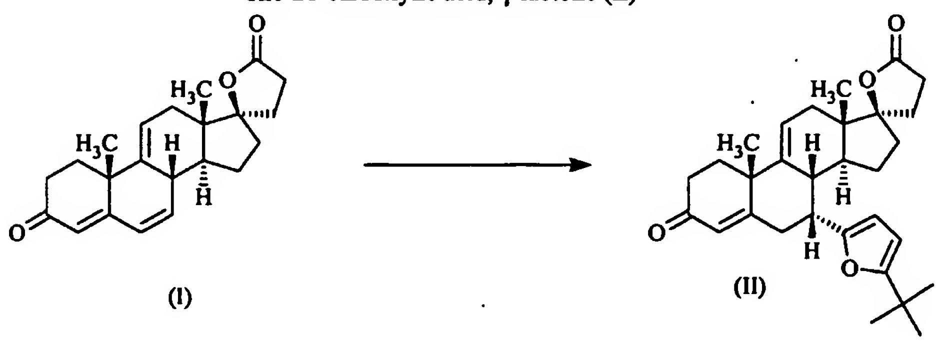
EXAMPLE 26 17β-Hydroxy-7α-carbomethoxypregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (VIII)



A mixture of 5α,17β-dihydroxypregn-9(11)-ene-3-one, 7α,21-dicarboxylic acid, bis-γ-lactone (VII, EXAMPLE 25, 50.0 g, 0.13005 moles) and potassium

bicarbonate (16.92 g, 0.1690 moles, 1.30 equivalents) in acetone (200 ml) and water (100 ml) is stirred at 45° for 2 hrs., at which time conversion of the 5,7-lactone (VII) into the carboxylic acid (VI) is complete by LC. The resulting mixture is then treated with dimethylsulfate (22.92 g, 0.1817 moles, 1.40 equivalents), stirred at 45° for 3 hrs., then treated with a solution of potassium bicarbonate (1.3 g, 0.0130 moles, 0.100 equivalents) in water (10 ml) followed by neat triethylamine (1.81 ml, 1.314 g, 0.0130 moles, 0.100 equivalents). The mixture is stirred at 45° for 1 hr., quenched with concentrated hydrochloric acid (1.92 ml, 2.304 g, containing 0.852 g (0.0234 moles, 0.180 equivalents) hydrochloric acid), cooled to 0°, concentrated under reduced pressure to a volume of 150 ml (pot temperature 13°), then filtered and the filter cake is washed with water (2 x 25 ml) and dried to give the title compound, by comparison with an authentic sample by LC.

EXAMPLE 27 17β-Hydroxy-7α-(5'-t-butyl-2'-furyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (II)

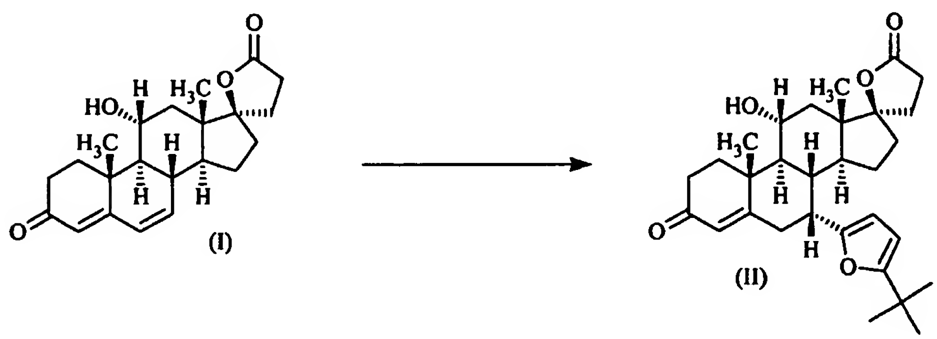


(I) (II)

A mixture of Δ^9-canrenone (I, 3.0002 g, 8.8645 mmoles) and 2-*t*-butylfuran (2.53 ml, 2.204 g, 17.745 mmoles, 2.00 equivalents) in nitromethane (12.0 ml) is treated with ethanol (0.52 ml, 413 mg, 8.96 mmoles, 1.01 equivalents), cooled to – 20°, and treated with boron trifluoride diethyl etherate (1.24 ml, 1.389 g, 9.785 mmoles, 1.10 equivalents). The resulting mixture is stirred at –20° for 24 hrs., then at –5° for 12 hrs., then at 0° for 4 hrs., at which time the reaction appeared about 90% complete by TLC. The reaction is quenched with ammonium hydroxide (7%, 30 ml) extracted with methylene chloride (3 x 50 ml), dried over magnesium sulfate, and concentrated. The concentrate is flash chromatographed on (silica gel, 150 g; gradient elution, 10% → 50% ethyl acetate/cyclohexane). The fractions containing pure product are combined and concentrated to give the title compound, CMR (100 MHz,

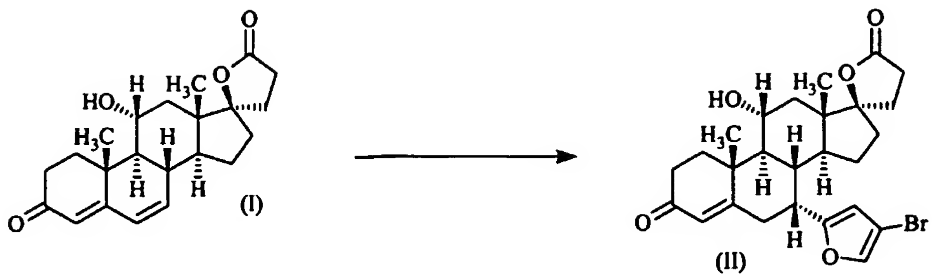
$CDCl_3$) 198.56, 176.53, 167.87, 162.48, 153.02, 142.91, 125.84, 119.42, 106.70, 101.88, 95.21, 44.05, 42.87, 41.90, 40.84, 38.17, 37.80, 35.52, 34.20, 34.02, 32.97, 32.40, 31.33, 29.18, 28.71, 26.79, 23.17 and 14.14 δ; NMR (400 MHz, $CDCl_3$) 0.95, 1.16, 1.45, 1.5 – 2.6, 2.94, 3.30, 5.64, 5.72 and 5.76 δ.

EXAMPLE 28 11α,17β-Dihydroxy-7α-(5'-t-butyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone (II)



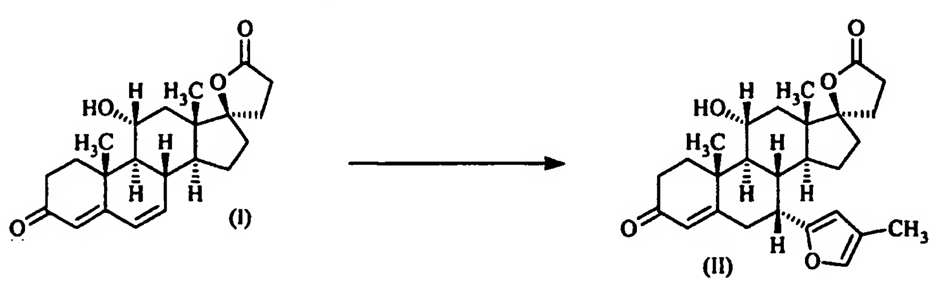
A mixture of 11α-hydroxycanrenone (I, 2.03 g, 5.6947 mmoles) and 2-*t*-butylfuran (1.70 ml, 1.481 g, 11.924 mmoles, 2.09 equivalents) in nitromethane (16 ml) is cooled to –20°, treated with ethanol (0.35 ml, 0.276 g, 5.99 mmoles, 1.05 equivalents) and boron trifluoride diethyl etherate (0.83 ml, 0.930 g, 6.550 mmoles, 1.15 equivalents), and stirred at –20° for 21 hrs., at which time LC analysis indicates that the reaction is complete. The reaction mixture is then quenched with ammonium hydroxide (15%, 5.5 ml), diluted with water, extracted with methylene chloride (2 x 25 ml), dried over magnesium sulfate, filtered through 5.0 g magnesol, and concentrated to a foam, which is flash chromatographed (silica gel, 200 g; gradient elution 20% → 70% ethyl acetate/cyclohexane). The fractions containing the product are combined and concentrated to give the title compound, UV λ_{max} = 238 mμ.

EXAMPLE 29 11α,17β-Dihydroxy-7α-(4'-bromo-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone (II)



A mixture of 11α-hydroxycanrenone (I, 2.0 g, 5.6425 mmoles), ethylene glycol (0.84 ml, 0.935 g, 15.06 mmoles, 2.67 equivalents), and 3-bromofuran (3.0 ml, 4.905 g, 33.372 mmoles, 5.91 equivalents) in nitromethane (32 ml) at 20-25° is treated with boron trifluoride diethyl etherate (1.4 ml, 1.568 g, 11.048 mmoles, 1.96 equivalents) and stirred at 20-25° for 20 hrs., at which time the reaction is > 80% complete by LC. The reaction is then quenched with water, extracted with ethyl acetate, and concentrated to give a foam, which is dissolved in methylene chloride (10 ml) and flash chromatographed (silica gel, 150 g; gradient elution 0 → 6% isopropanol/methylene chloride). The product-containing fractions are then combined and rechromatographed (silica gel, 100 g silica gel; gradient elution 0 → 5% isopropanol/methylene chloride). The product-containing fractions are combined and crystallized from ethyl acetate/cyclohexane (1/2) to give the title compound, CMR (100 MHz, $CDCl_3$) 199.77, 176.54, 168.67, 152.83, 142.43, 126.05, 113.41, 98.03, 95.02, 69.19, 53.51, 46.26, 46.19, 43.40, 39.57, 38.72, 38.05, 37.48, 35.39, 34.77, 34.24, 31.09, 29.11, 22.68, 18.46 and15.84 δ; NMR (400 MHz, $CDCl_3$) 0.9 – 2.9, 1.03, 1.42, 3.35, 4.11, 6.36 and 7.26 δ; MS (CI, NH_3) m/e = 503, 505 (100%, P + H).

EXAMPLE 30 11α,17β-Dihydroxy-7α-(4'-methyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone (II)



A mixture of 11α-hydroxycanrenone (I, 816 mg, 2.2891 mmoles) and 3-methylfuran (4.0 ml of 1.218 M solution in nitromethane, 4.87 mmoles, 2.13

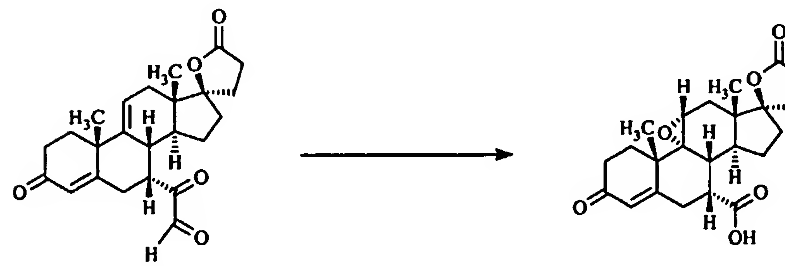
equivalents) in nitromethane (4.0 ml) is cooled to –20° and treated with ethylene glycol (0.168 ml, 187 mg, 3.01 mmoles, 1.32 equivalents) followed by boron trifluoride diethyl etherate (0.284 ml, 318 mg, 2.241 mmoles, 0.98 equivalents). The resulting mixture is stirred at –20° for 20 hrs., at which time the reaction is 86% complete by LC. The reaction mixture is quenched with aqueous ammonium hydroxide (15%, 4 ml) diluted with water (10 ml), extracted with methylene chloride (2 x 20 ml), dried over magnesium sulfate, and concentrated. The concentrate is flash chromatographed (silica gel, 60 g; gradient elution 50% → 100% ethyl acetate/cyclohexane). The product-containing fractions are combined and concentrated. The concentrate is crystallized from cyclohexane/ethyl acetate (4/1) to give the title compound, CMR (100 MHz, $CDCl_3$) 199.91, 176.62, 170.02, 150.94, 140.81, 125.57, 115.27, 112.29, 95.07, 69.16, 53.50, 46.13, 45.99, 43.24, 39.52, 39.46, 38.14, 37.35, 35.32, 34.18, 31.05, 29.07, 22.28, 18.46, 15.79 and 10.21 δ; NMR (400 MHz, $CDCl_3$) 1.04, 1.0 – 2.9, 1.42, 1.96, 3.14, 4.12, 5.34, 6.12 and 7.15 δ; MS (CI, NH_3) m/e = 439 (100%, P + H).

EXAMPLE 31 17β-Hydroxy-7α-(5'-methyl-2'-furyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (II)

Ishikawa reagent (2.4 mK, 13.7 mmol) is added to a mixture of 11α,17β-dihydroxy-7α-(5'-methyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone (II, EXAMPLE 12, 5 g, 11.4 mmol) in acetonitrile (25 mL). The mixture is heated to 60° and is determined complete in 1 hr by HPLC. The resulting mixture is cooled to 22° and quenched with saturated aqueous sodium bicarbonate (15 mL). The organic solvent is removed under reduced pressure and replaced with methylene chloride (50 mL). The organic phase is separated, washed with water (30 mL) and concentrated to a volume of 20 mL. Water (30 mL) is added and the mixture is concentrated to a volume of 20 mL. This water distillation is repeated twice to remove the N,N-diethyl-2,3,3,3-tetrafluoropriopionamide by-product. Then, methylene chloride (30 mL) is added to the resulting slurry to dissolve all solids. The organic layer is separated and the solvent is exchanged to *n*-propyl acetate to a final volume of 17-18 mL. The resulting slurry is cooled to –20° for 12 hours. The product was collected by filtration and dried under ambient nitrogen to give the title compound, mp = 198-203°; NMR (400 MHz, $CDCl_3$) 5.737, 5.690, 3.300, 2.904, 2.164, 1.431, 0.952 and 2.569-1.358 δ;

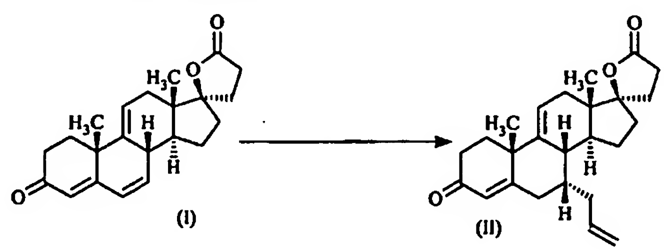
CMR (100 MHz, $CDCl_3$) 198.5, 176.5, 167.4, 152.7, 150.0, 142.8, 126.2, 119.7, 107.1, 105.9, 95.2, 44.1, 42.4, 41.9, 38.5, 37.6, 35.4, 33.9, 32.9, 31.3, 29.1, 26.8, 23.2, 14.1 and 13.4 δ; MS calculated for $C_{27}H_{33}O_4$ = 421.238 (M + H^+), found = 421.2 m/z.

EXAMPLE 32 9α,11α-Epoxy-17β-hydroxypregn-4-en-3-one-7α,21-dicarboxylic acid, γ-lactone (VI)



A mixture of 17β-hydroxy-7α-(2'-oxoacetyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (V, EXAMPLE 11, 6.7 mg, 0.0169 mmoles) in methylene chloride (0.5 ml) is treated with peracetic acid (35%, 4 μl, containing 1.58 mg, 0.0208 mmoles, 1.23 equivalents of peracetic acid), stirred at 20-25° for 25 hours, then treated with more peracetic acid (35%, 2 μl, containing 79 mg, 0.0104 mmoles, 0.62 equivalents of peracetic acid), then stirred at 20-25° for 49 hrs., at which time LC analysis indicated conversion to the title compound, LC-UV (λ_{max} = 244 nm); LC-MS (m/e 400).

EXAMPLE 33 7α-Allyl-17β-hydroxypregna-4,9(11)-dien-3-one, 21-carboxylic acid, γ-lactone (II)



A mixture of 17β-hydroxypregna-4,6,9(11)-trien-3-one-21-carboxylic acid, γ-lactone (I, 1.0171 g, 3.0052 mmoles) in methylene chloride (62 ml) is cooled to –30° and treated with titanium tetrachloride in methylene chloride (1.0 M, 15.0 ml, 15.0 mmoles, 4.99 equivalents). The resulting mixture is treated with allyltrimethylsilane (3.0 ml, 2.16 g, 18.876 mmoles, 6.28 equivalents) and stirred at –30° for 4 hrs., at which time conversion of the starting material into the product (R_f = 0.27) is nearly

complete by TLC (ethyl acetate/cyclohexane, 35/65). The reaction mixture is quenched with water (25 ml), extracted with methylene chloride (3 x 25 ml), and concentrated. The concentrate (weight = 1.6262 g) is flash chromatographed (silica silica gel, 150 g; gradient elution with ethyl acetate/cyclohexane, 15% → 55%). The fractions containing the more polar product (R_f = 0.27) are combined and concentrated to give the title compound, UV λ_{max} = 241 nm; CMR (100 MHz, $CDCl_3$) 198.65, 176.46, 167.31, 143.22, 136.36, 126.51, 119.84, 116.80, 95.22, 44.15, 42.50, 41.13, 40.73, 37.33, 35.56, 35.43, 34.13, 33.78, 33.05, 31.65, 31.37, 29.14, 26.86, 23.04, and 13.78 δ; NMR (400 MHz, $CDCl_3$) 0.94, 1.37, 1.4 – 2.6, 4.95, 5.01, 5.65 and 5.74 δ; MS (CI, NH_3), m/e = 381 (P + H, 100%);

The product is rechromatographed (silica gel, 60 g; gradient elution with ethyl acetate/cyclohexane, 15% → 45%) to remove a more polar impurity (R_f = 0.06). The product-containing fractions are combined and concentrated. A portion of the residue (96.8 mg) is taken up in methylene chloride (1 ml), diluted with ethyl acetate (2 ml), concentrated to a volume of less than 1 ml, and cooled to 0°. The supernatant is decanted and the crystals recrystallized from ethyl acetate at 0°. An X-ray crystallographic study confirmed the assignment as 7α-allyl-17β-hydroxypregna-4,9(11)-dien-3-one, 21-carboxylic acid, γ-lactone.

EXAMPLE 34 5α,17β-Dihydroxypregn-9(11)-ene-3-one, 7α,21-dicarboxylic acid, bis-γ-lactone (VII)

Step (1) - 17β-Hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone (VI)

A mixture of 17β-hydroxy-7α-(5'-methyl-2'-furyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone (II, EXAMPLE 3, 20 g, 47.5568 mmoles) in methanol (60 ml) and methylene chloride (60 ml) is cooled to –55°. Ozone in oxygen is bubbled through this mixture until 0.8 area % (by LC) of starting material (II) remains. The mixture is purged of ozone by sparging with nitrogen and then quenched with dimethylsulfide (16 ml, 13.5 g, 217.9 mmoles, 4.58 equivalents), warmed to 20-25°, stirred at 20-25° for 50 min. The resulting mixture is concentrated to 80 ml, methanol (25 ml) is added, and concentrated to 80 ml again. The mixture is then treated, at 5°, with a solution of potassium bicarbonate (21.6g; 215.7 mmoles; 4.54 equivalents) in water (44 ml) followed by hydrogen peroxide (50% aqueous, 23.5

g, containing 11.75 g (345.5 mmoles, 7.27 equivalents) of hydrogen peroxide). After warming to 20-30° for one hour the mixture is quenched with dimethylsulfide (8 ml, 6.75 g, 108.95 mmoles, 2.29 equivalents). Methylene chloride (20 ml) is added, and the pH adjusted to 3 with hydrogen chloride (31.5% aqueous, 26.0g containing 8.19g (224.4 mmoles; 4.72 equivalents) of hydrogen chloride. The mixture is warmed to dissolve and the phases separated. The upper aqueous phase is extracted with methylene chloride (10 ml) and the combined organic phases are extracted with water (10 ml.). LC was performed on the methylene chloride mixture (after aqueous workup) under the following conditions:

Column:	Supelco Discovery RP Amide C16; 5 μ; 250 mm x 4 mm
Flow:	1 ml/min
Detection:	UV; 240 nm
Mobile Phase:	A: 950 g Water; 39 g Acetonitrile; 1.0g Trifluoroacetic acid B: 754 g Acetonitrile; 39 g Water; 1.0g Trifluoroacetic acid
Gradient:	T_0: 80% A/20%B T_{15}: 20% A/80%B $T_{15.1}$: 80% A/20%B T_{20}: 80% A/20%B
Run Time:	20 minutes
Flow:	1 ml/min
Injection Volume:	5 λ
Sample Prep:	5 λ or reaction mixture into 1ml of 1/1 Acetonitrile: phosphate buffer (1 ml phosphoric acid in 1 l water; pH to 2.4 with sodium hydroxide)

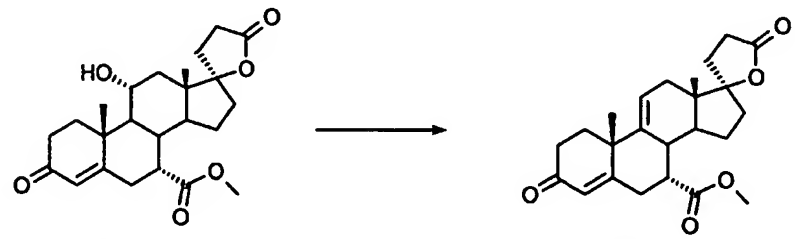
The reaction LC major peak (72 area %) was at 10.52 minutes; retention time of a known standard of the carboxylic acid (VI) is 10.52 minutes.

Step (2) - 5α,17β-Dihydroxypregn-9(11)-ene-3-one, 7α,21-dicarboxylic acid, bis-γ-lactone (VII)

The resulting organic phase containing 17β-hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone (VI) is concentrated to 40 ml and para-toluene sulfonic acid monohydrate (10 mg; 0.042 mmoles; 0.001 equivalents) dissolved in acetone (15 ml) is added. Crystallization is observed after 30 minutes at reflux. The resulting slurry is concentrated to 50 ml and concentration continued while maintaining a constant volume by the addition of fresh acetone. After 80 ml of acetone has been added the slurry is cooled to 0° and the solids collected by filtration to give the title compound, CMR (100 MHz, $CDCl_3$) 206.07, 176.44, 175.41, 139.66,

123.98, 94.88, 90.99, 47.09, 43.91, 42.36, 41.57, 41.08, 38.93, 36.98, 35.17, 33.01, 32.44, 31.36, 29.10, 23.08, 22.99 and 14.24 δ; NMR (400 MHz, $CDCl_3$) 0.94, 1.41, 1.5 – 2.6, 2.80 and 5.70 δ.

EXAMPLE 35 17β-hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester (CII)



(CI) (CII)

11α,17β-dihydroxypregn-4-en-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester (CI, *Drugs of the Future*, 24(5), 488-501 (1999), compound (VI) and International Publication WO98/25948, pages 76 and 280; 5.00 g, 12.0 mmol) is mixed with acetonitrile (15 ml). N-(1,1,2,3,3,3)hexafluoropropyl)-diethylamine (CVI, 2.55 ml, 14.4 mmol) is added to this the steroid mixture and heated to 60° for 2.5 hours. The resulting mixture is cooled to 20-25° and the reaction is quenched with methanol (100 μL). A saturated aqueous solution of potassium bicarbonate (15 ml) is added. The acetonitrile is then removed under reduced pressure. The resulting mixture is extracted with methylene chloride (3 x 10 ml). The combined organic phases are washed with a aqueous solution of sodium chloride (10%, 20 ml). The solvent is dried with magnesium sulfate. The solvent is exchanged from methylene chloride to methyl *t*-butyl ether (MTBE). The mixture is concentrated to a final volume of 25 ml. The resulting slurry is stirred overnight and the final product, the title compound, is collected by filtration.

EXAMPLE 36 17β-hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester (CII)

11α,17β-dihydroxypregn-4-en-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester (CI, 5.00 g, 12.0 mmol) is placed in a flask with acetonitrile (15ml). To this mixture the Ishikawa reagent (2.55 ml, 14.4 mmol) is added and heated to 60° for 2 hrs. The mixture is cooled to 20-25° and the reaction is quenched with aqueous potassium bicarbonate (20% solution, 18 ml). The acetonitrile is removed under

reduced pressure, the aqueous layer is extracted with methylene chloride (3 x 5 ml). The combined organic phases are washed with sodium chloride solution (10%, 10ml). The solvent is exchanged from methylene chloride to methyl isobutyl ketone/heptane to crystallize the title compound, mp = 198.6-199.5°; MS (m/z) calculated for $C_{24}H_{30}O_5$ = 398.5 (M+), found 398.9(M+); NMR ($CDCl_3$) 5.69, 5.64, 3.62, 2.97, 2.84-1.47, 1.38 and 0.93 δ; CMR ($CDCl_3$) 98.5, 176.4, 172.5, 166.5, 142.3, 125.6, 118.9, 95.0, 51.3, 43.0, 40.3, 35.6, 35.2, 34.1, 33.7, 32.8, 31.2, 29.0, 27.1, 23.2 and 14.0 δ.

EXAMPLE 37 17β-hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester (CII)

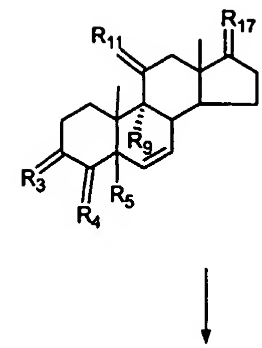
11α,17β-dihydroxypregn-4-en-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester (CI, 80.00 g, 192.1mmol) is placed in a flask with acetonitrile (80 ml). To this mixture the Ishikawa reagent (40.8 ml, 224.8 mmol) is added and heated slowly to 45 to 50°, then held for 1-2 hours. The mixture is cooled to 20-25° and the reaction is quenched with aqueous potassium bicarbonate (72 g in 288 ml). Methylene chloride (240 ml) is added and after mixing the layers are separated. The aqueous phase is extracted with methylene chloride (100 ml). The combined organic phases are washed with water (240 ml). The solvent is exchanged from methylene chloride to methyl *tert*-butyl ether, and branched octane is added drop wise to crystallize the product which is the title compound.

EXAMPLE 38 17β-hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester (CII)

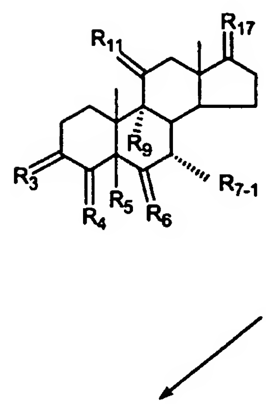
11α,17β-dihydroxypregn-4-en-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester (CI, 80.00 g, 192.1 mmol) is placed in a flask with acetonitrile (80 ml). To this mixture the Ishikawa reagent (40.8 ml, 224.8 mmol) is added and heated slowly to 55 to 50°, then held for 1-2 hours. The mixture is cooled to 20-25° and the reaction is quenched with aqueous potassium bicarbonate (37.3 g in 288 ml). Methylene chloride (240 ml) is added and after mixing the layers are separated. The aqueous phase is extracted with methylene chloride (100 ml). The combined organic phases are washed with water (80 ml). The solvent is exchanged from methylene chloride to methyl *iso*-butyl ketone, and branched octane is added drop wise to crystallize the product which is the title compound.

CHART A

When R_{7-1} is (-A1)



(I)



(II)

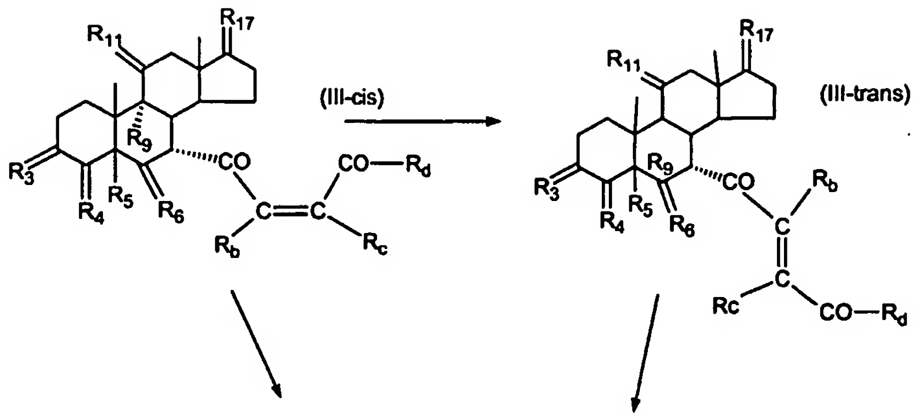
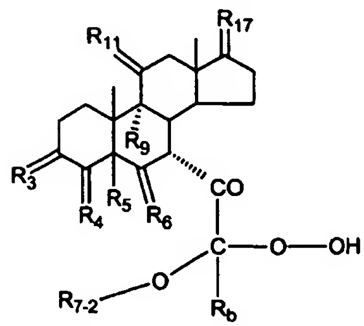
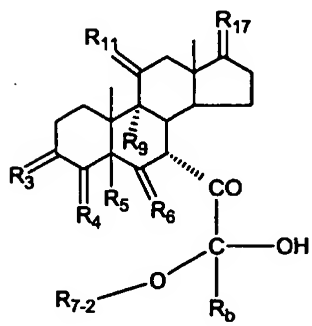


CHART A - Continued



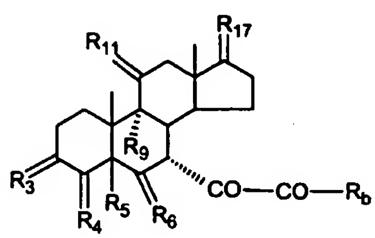
(IV-OOH)

+



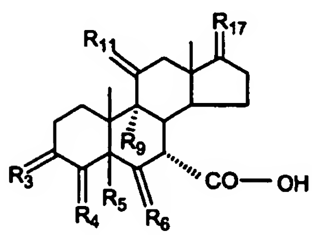
(IV-OH)

+



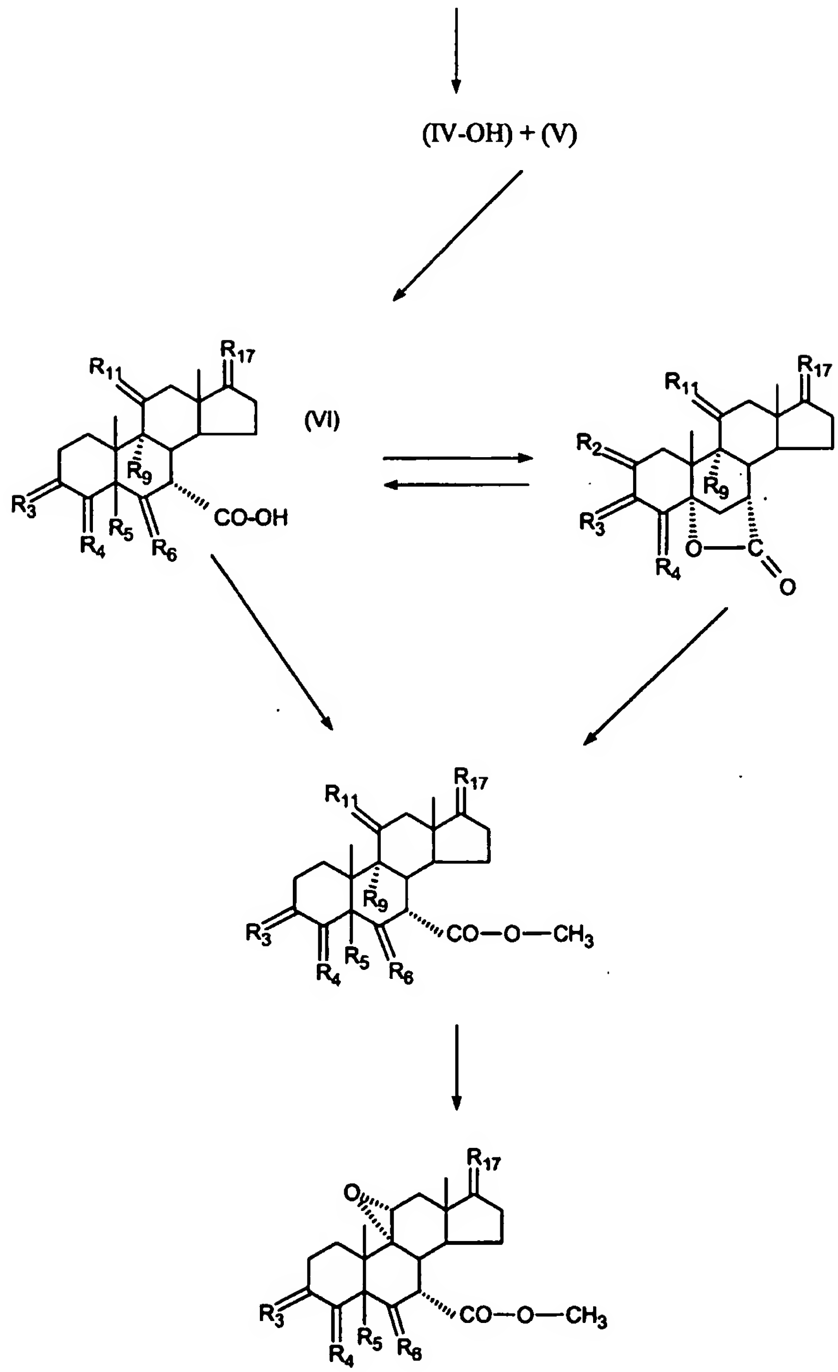
(V)

+



(VI)

CHART A - Continued



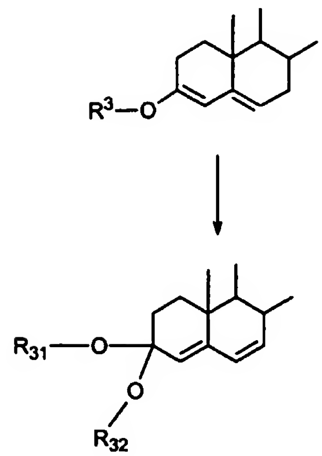
(VI)

(VII)

(VIII)

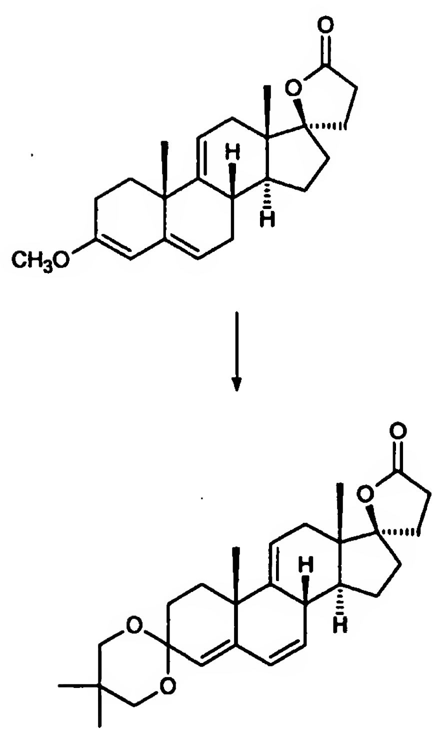
(IX)

CHART B



(Alkyl enol ether)

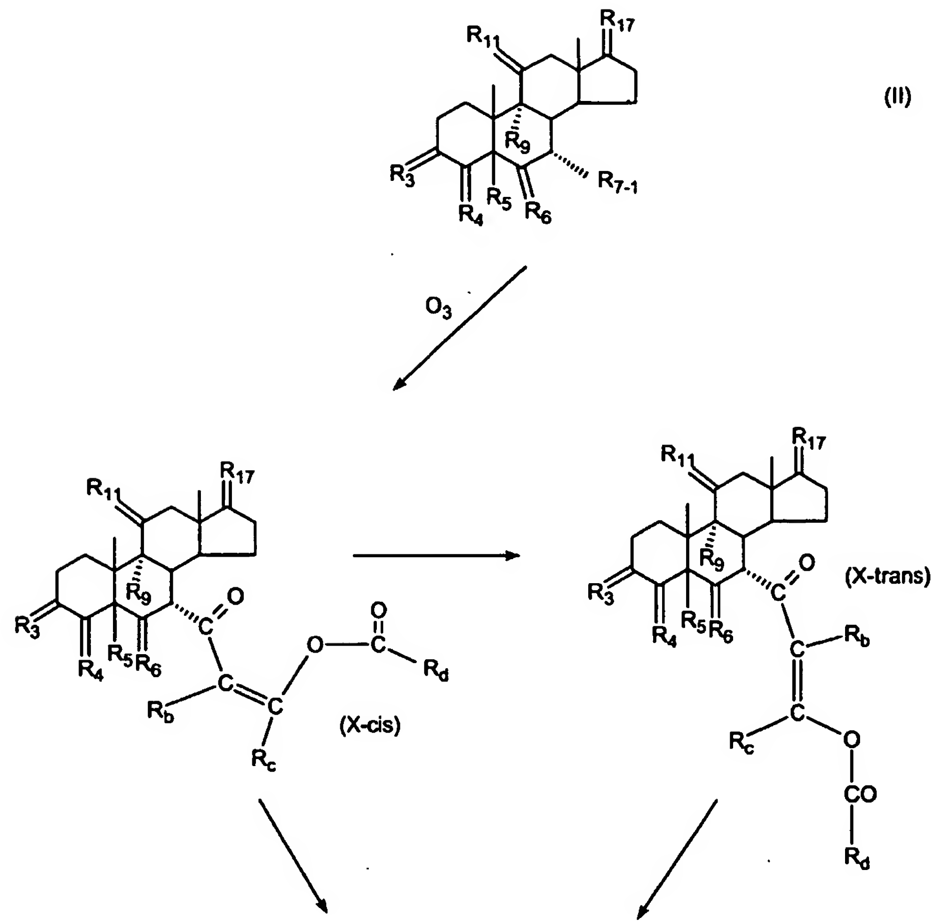
(I-P)



(3-methyl enol ether)

(I-P')

CHART C



(IV-OOH) + (IV-OH) + (V) + (VI)

↓

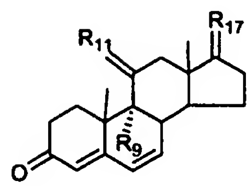
Following the general procedure of CHART A and D

↓

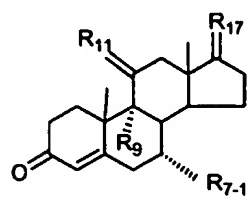
(IX)

CHART D

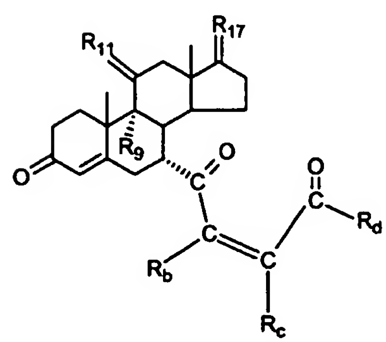
When R_{7-1} is (-A1)



(I-unprotected A-ring)

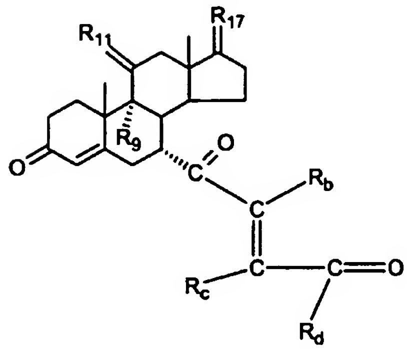


(II-unprotected A-ring)



(III-cis-unprotected A-ring)

CHART D – Continued

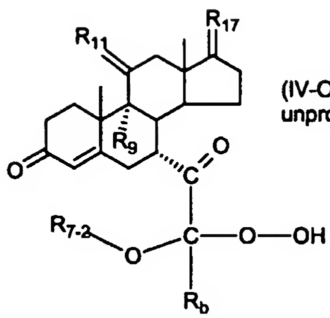


(III-trans-unprotected A-ring)

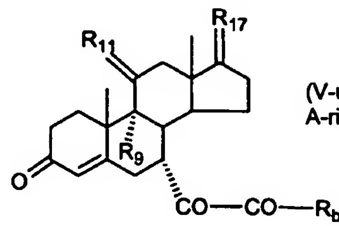
CHART D – Continued

(III-*cis*) or (III-*trans*) or mixture of (III-*cis*) and (III-*trans*)

↓

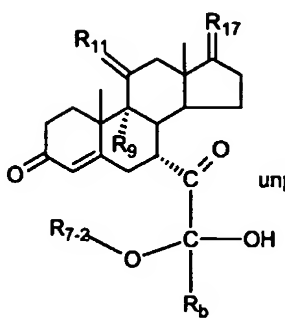


(IV-OOH- unprotected A-ring) +



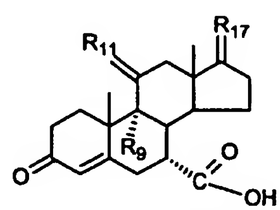
(V-unprotected A-ring)

+



(IV-OH- unprotected A-ring)

+



(VI-unprotected A-ring)

↓

(IV-OH unprotected A-ring) + (V-unprotected A-ring) + (VI-unprotected A-ring)

CHART D – Continued

(IV-OH unprotected A-ring) + (V unprotected A-ring)

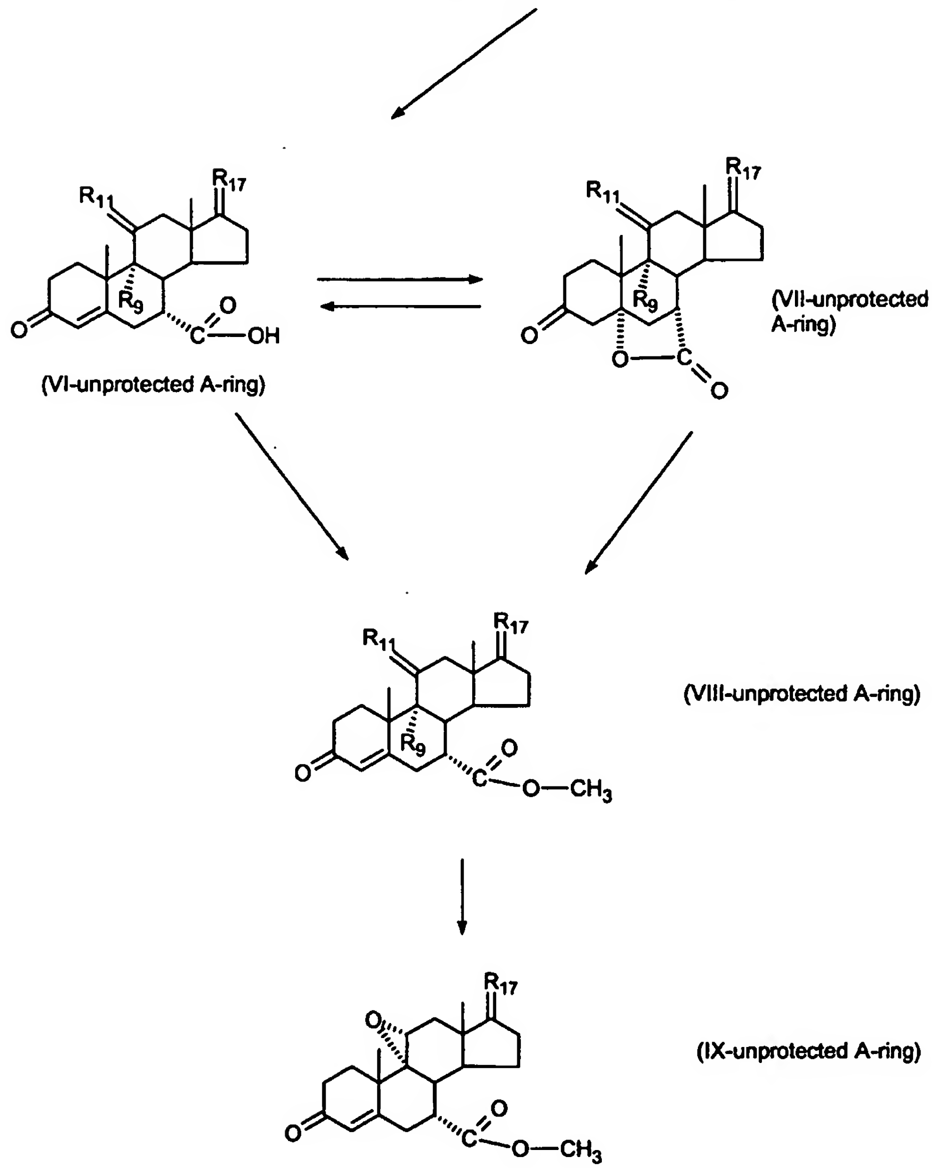
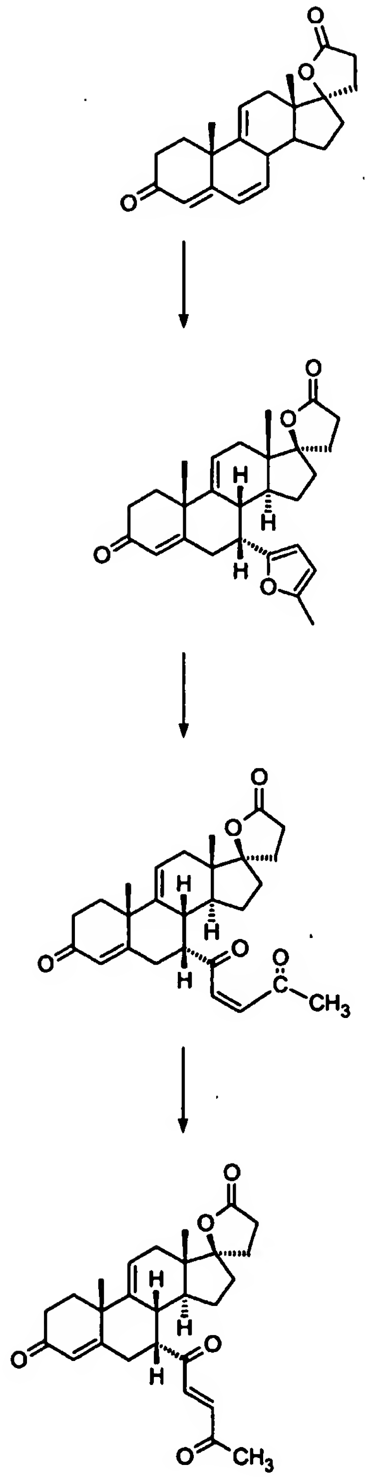


CHART E



(I)

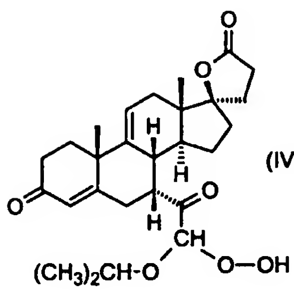
(II)

(III-cis)

(III-trans)

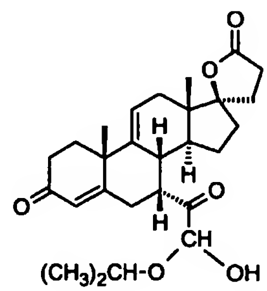
CHART E - Continued

(III-*cis*) or (III-*trans*) or mixture of (III-*cis*) or (III-*trans*)



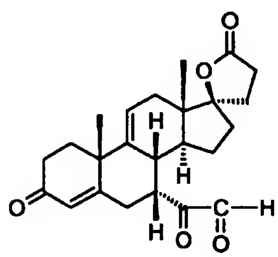
(IV-OOH)

+



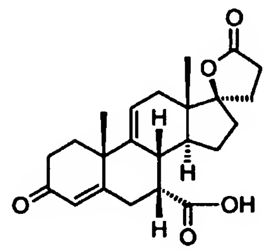
(IV-OH)

+



(V)

+



(VI)

(IV-OH) + (V) + (VI)

CHART E – Continued

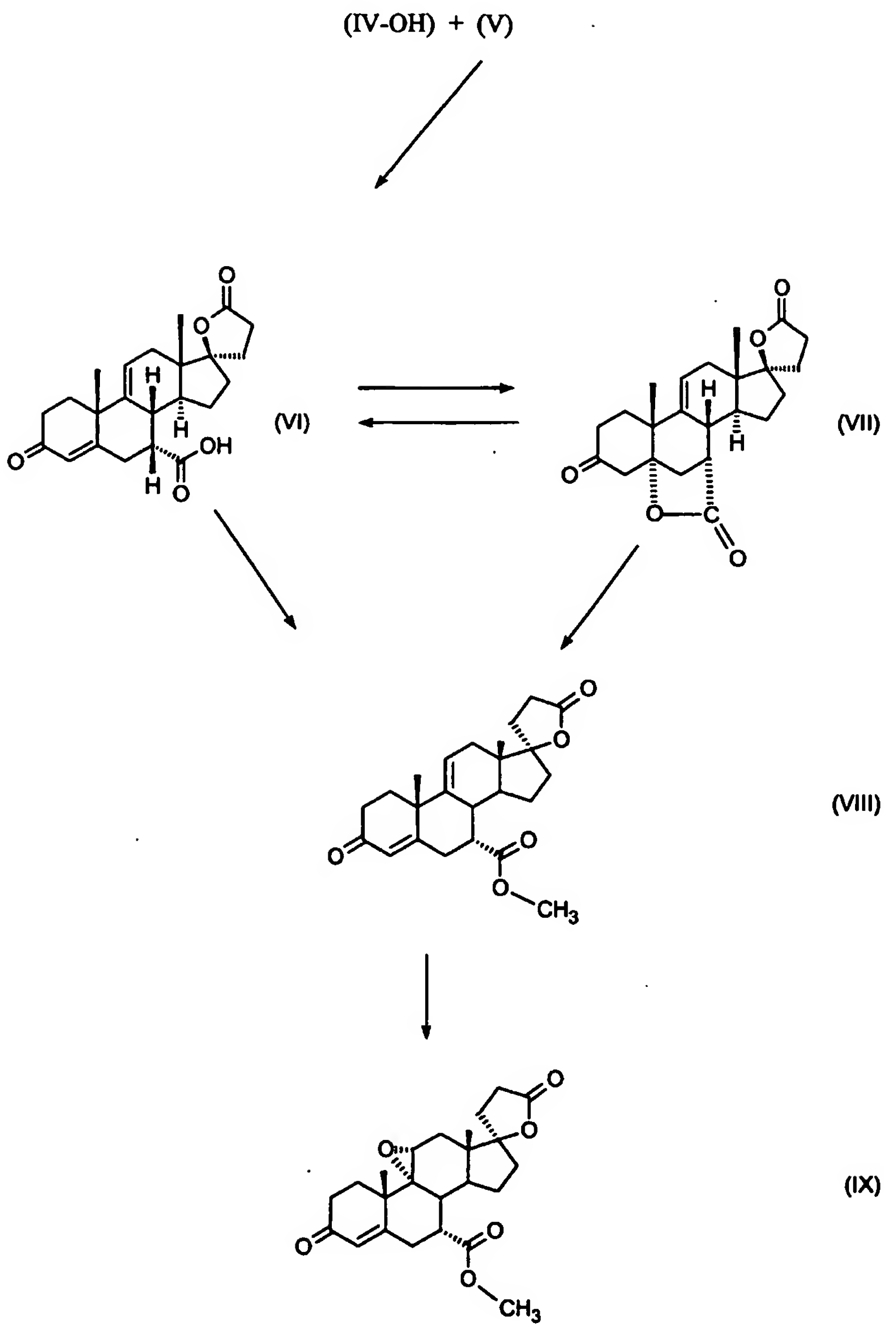
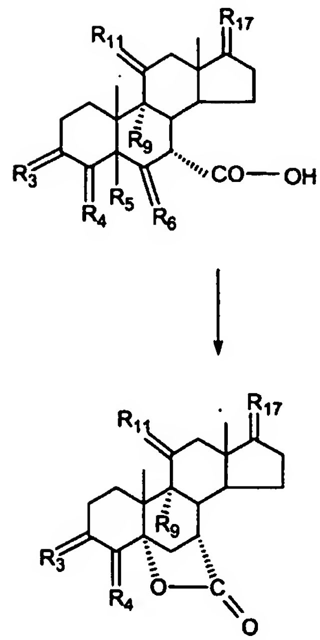
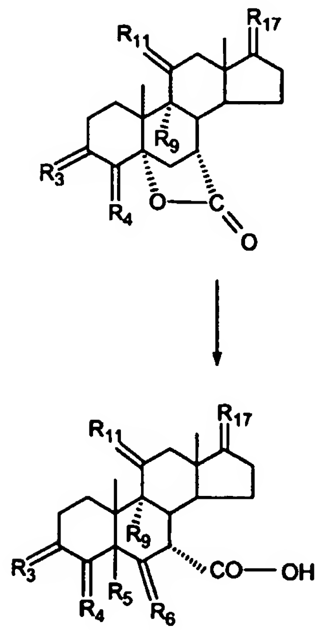


CHART F



(VI)

(VII)

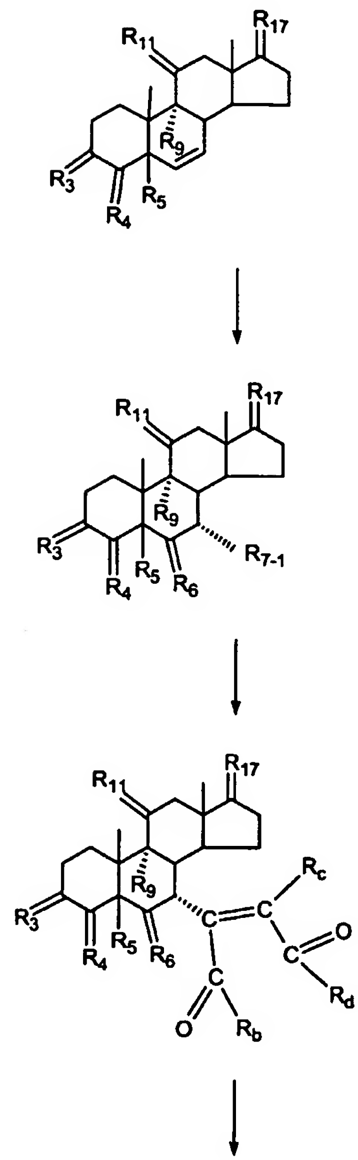


(VII)

(VI)

CHART G

When R_{7-1} is (-A2)

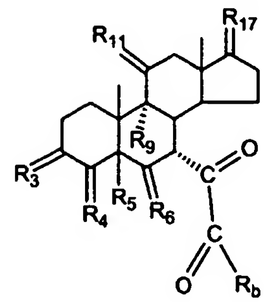


(I)

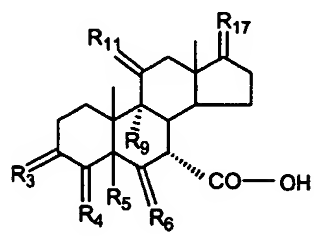
(II)

(XIV)

CHART G - Continued



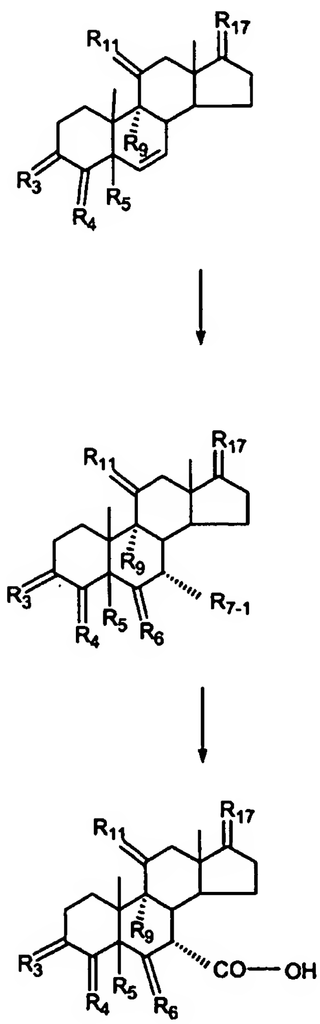
(XV)



(VI)

CHART H

When R_{7-1} is (-B), (-C) or (-D1, -D2, -D3)

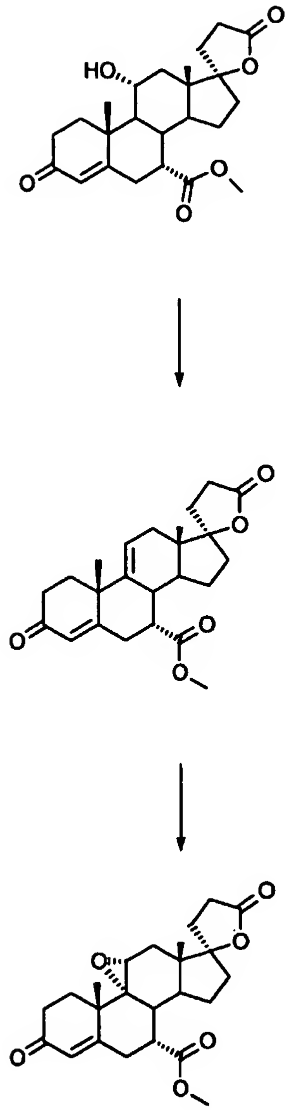


(I)

(II)

(VI)

CHART I

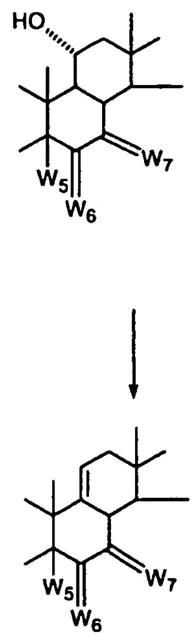


(CI)

(CII)

(CIII)

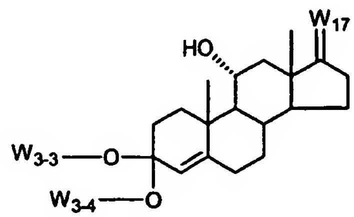
CHART J

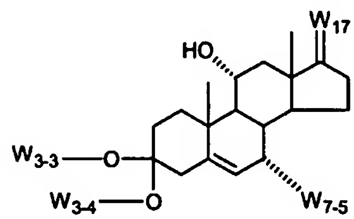


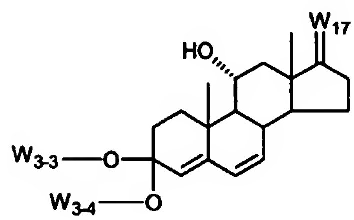
(CIV)

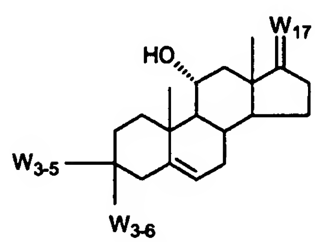
(CV)

CHART K


W17
HO
W3-3
O
W3-4
O


W17
HO
W3-3
O
W3-4
O
W7-5


W17
HO
W3-3
O
W3-4
O


W17
HO
W3-5
W3-6

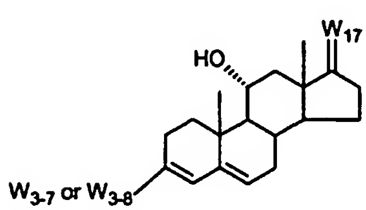
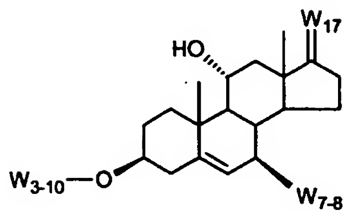
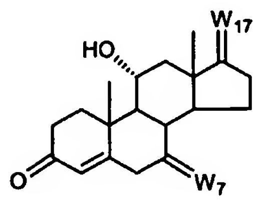
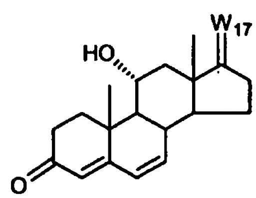
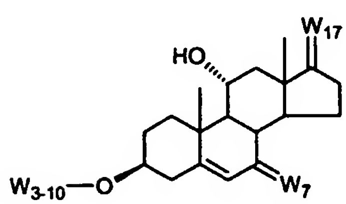

W17
HO
W3-7 or W3-8

CHART K - Continued









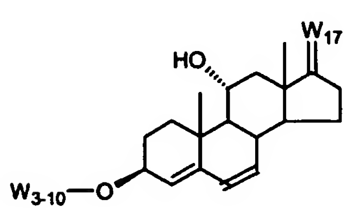
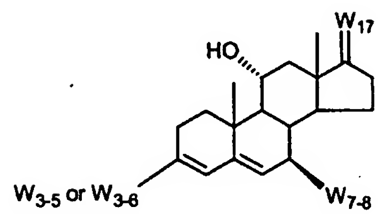
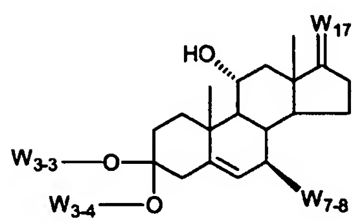


CHART K – Continued





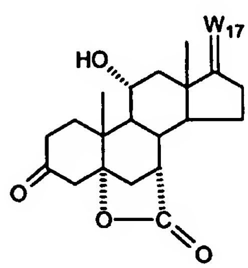
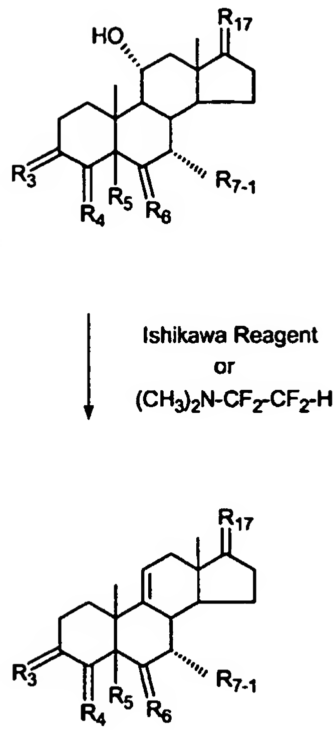


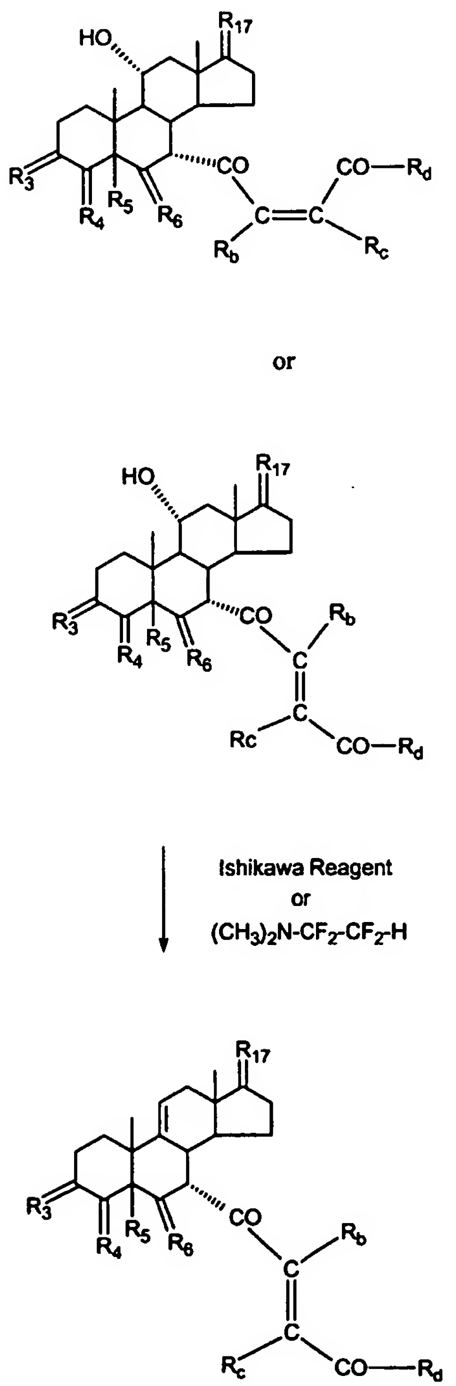
CHART L



(II)

(II)

CHART M

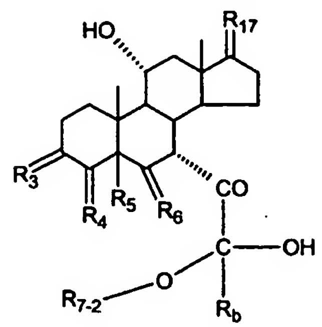


(III-cis)

(III-trans)

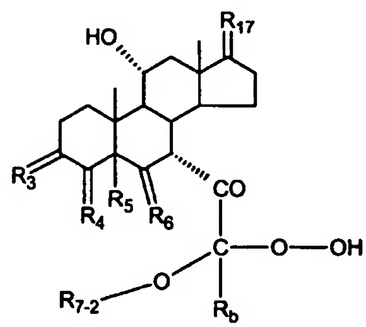
(III-trans)

CHART N



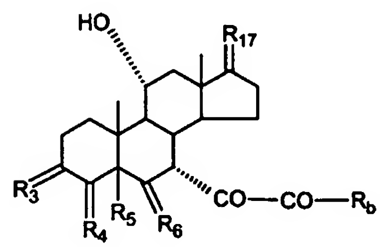
(IV-OH)

or



(IV-OOH)

or



(V)

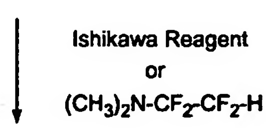
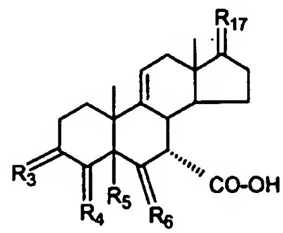
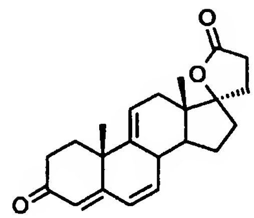


CHART N – Continued



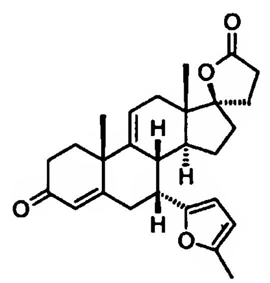
(VI)

CHART O



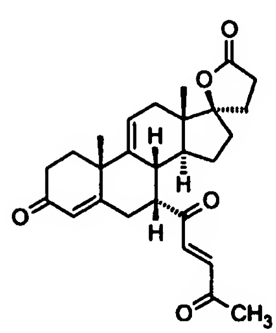
(I)

2-methylfuran
absolute ethanol
boron trifluoride etherate



(II)

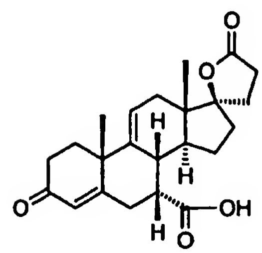
dibromatin
acetate
aqueous hydrochloric acid



(III-trans)

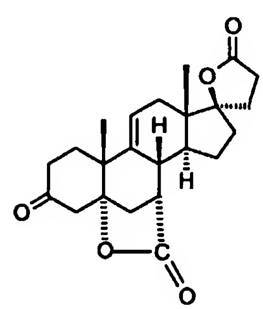
CHART O – Continued

ozone
dimethylsulfide
hydrogen peroxide
bicarbonate



(VI)

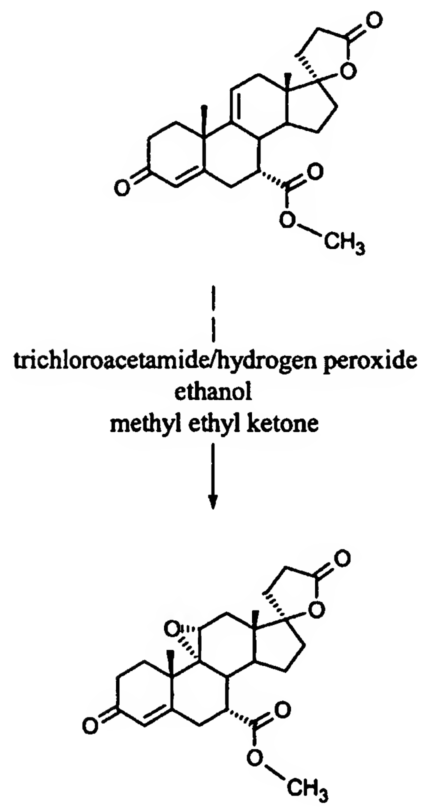
p-toluenesulfonic acid



(VII)

bicarbonate
dimethylsulfate

CHART O – Continued

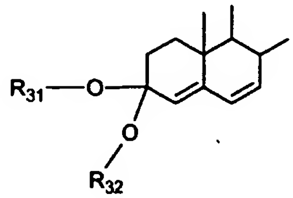


(VIII)

(IX)

CLAIMS

1. A process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P)



(I-P)

where R_{31} and R_{32} are

(1) the same or different and are C_1-C_3 alkyl, and

(2) taken with the attached -O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

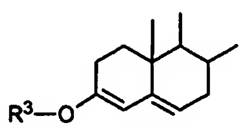
where R_{33} and R_{34} are the same or different and are

-H,

C_1-C_3 alkyl,

which comprises

(1) contacting a $\Delta^{3,5}$-3-enol ether of formula (Alkyl enol ether)



(Alkyl enol ether)

where R^3 is

C_1-C_3 alkyl,

CH_3-CO-,

Φ-CO- or

$R_{Si-1}R_{Si-2}R_{Si-3}Si$- where R_{Si-1}, R_{Si-2} and R_{Si-3} are the same or different and are C_1-C_4 alkyl; with a hydride abstractor and an alcohol selected from the group consisting of alcohols of the formula:

(a) R_{31}-OH, where R_{31} is as defined above,

(b) R_{32}-OH, where R_{32} is as defined above,

(c) HO-(CH_2)-$(CR_{33}R_{34})_{n1}$-(CH_2)-OH where n_1, R_{33} and R_{34} are as defined above,

(d) HO-CH_2-CH_2-OH.

2. A process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P) according to claim 1 where R^3 is C_1 alkyl.

3. A process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P) according to claim 1 where R_{31} and R_{32} are cyclized to form a group selected from the group consisting of

$-CH_2-C(CH_3)_2-CH_2-$ known as 2,2-dimethylpropane-1,3-diyl,

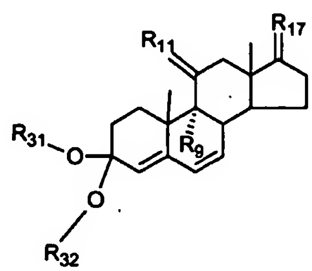
$-CH_2-C(CH_3CH_2)_2-CH_2-$ known as 2,2-diethylpropane-1,3-diyl,

$-CH_2-CH_2-$ known as ethane-1,2-diyl,

$-CH_2-CH_2-CH_2-$ known as propane-1,3-diyl.

4. A process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P) according to claim 3 where R_{31} and R_{32} are cyclized to form $-CH_2-CH_2-$ or $-CH_2-C(CH_3)_2-CH_2-$.

5. A process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P) according to claim 1 where the $\Delta^{4,6}$-ketal (I-P) is of the formula



(I-P)

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of

$-Si(-CH_3)_3$,

$-Si(-CH_2-CH_3)_3$,

$-CO-CH_3$,

-CO-H and

-SiH(CH_3)$_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above, and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above, with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H, where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si(R_{17-1-2})$_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) $-C\equiv C-CH_2-O-$(HYDROXY PROTECTING GROUP),

where HYDROXY PROTECTING GROUP is as defined above,

(f) $-CH_2-CH_2-CH_2-OH$,

(g) $-CH_2-CH_2-CH_2-O-$(HYDROXY PROTECTING GROUP),

where HYDROXY PROTECTING GROUP is as defined above

(h) $-CH_2-CH_2-CO-O^-$ and where R_{17-2} is $-OH$;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is $-OH$ and where R_{17-4} is:

(a) $-CO-CH_3$,

(b) $-CO-CH_2-OH$,

(c) $-CO-CH_2-O-CO-(CH_2)_{0-3}-CH_3$;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing $-O-CH_2-$ where the attachment of the $-O$ is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the $-O$ is at R_{17-8} in the β-orientation;

(6) $-O-CH(OR_{17-9})-CH_2-CH_2\cdots\cdots$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group ($CH_2\cdots\cdots$) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is $-H$ or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}-CH=CH_2$ and R_{17-12} is $-OH$.

6. A process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P) according to claim 5 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is $-H$;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

7. A process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P) according to claim 6 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

8. A process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P) according to claim 5 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

9. A process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P) according to claim 8 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

10. A process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P) according to claim 1 where the hydride abstractor is selected from the group consisting of

DDQ,

p-chloranil,

o-chloranil,

Mn^{+3}, Mn^{+7}, Pb^{+4}, Pd^{+2}, Ru^{+8}, Cr^{+6},

o-iodoxybenzoic acid,

o-iodoxybenzoic acid complex with DMSO,

o-iodoxybenzoic acid complex with

4-methoxypyridine-N-oxide,

N-methylmorpholine-N-oxide,

trimethylamine-N-oxide,

iodic acid (HIO_3),

iodine pentoxide (I_2O_5),

ceric ammonium nitrate,

iodosobenzene,

iodobenzenebistrifluoroacetate,

iodobenzenediacetate,

tritylfluoroborate,

and by electrochemical oxidation with a catalytic amount of a hydride abstractor.

11. A process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P) according to claim 10 where the hydride abstractor is DDQ, *p*-chloranil, manganese dioxide, manganic acetate, lead tetraacetate, chromium trioxide-dimethylpyrazole, chromium trioxide-pyridine, palladium acetate and ruthenium trichloride/*t*-butylhydroperoxide.

12. A process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P) according to claim 10 where the hydride abstractor is DDQ.

13. A process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P) according to claim 10 where the process is performed under essentially anhydrous conditions.

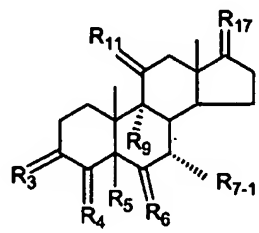
14. A process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P) according to claim 1 where the alcohol is neopentylglycol .

15. A process for the preparation of a $\Delta^{4,6}$-ketal of formula (I-P) according to claim 1 where the steroid is selected from the group consisting of

17β-hydroxypregna-4,6,9(11)-trien-3-one-21-carboxylic acid, γ-lactone, cyclic 3-(2',2'-dimethyl-1',3'-propanediyl ketal),

17β-hydroxypregna-4,6,9(11)-trien-3-one-21-carboxylic acid, γ-lactone, cyclic 3-ethanediyl ketal.

16. A 7α-substituted steroid of formula (II)



(II)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(II) R_3 is R_{3-3}:R_{3-4} and R_4 is R_{4-3}:R_{4-4} where one of R_{3-3} and R_{3-4} is –O-R_{31} where R_{31} is C_1-C_3 alkyl, the other of R_{3-3} and R_{3-4} is taken together with one of R_{4-3} and R_{4-4} to form a second bond between the carbon atoms to which they are attached, and the other of R_{4-3} and R_{4-4} is –H; R_6 is R_{6-3}:R_{6-4} where one of R_{6-3} and R_{6-4} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-3} and R_{6-4} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

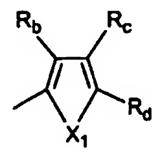
$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

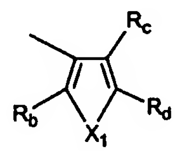
(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is $-O-R_{31}$ and R_{3-8} is $-O-R_{32}$ where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_{7-1} is a molecular fragment of the formula (-A1)



(-A1)

or of the formula (-A2)



(-A2)

where X_1 is:

–S-,

-O- or

–NX_{1-1}- and where X_{1-1} is:

-H,

C_1-C_4 alkyl,

-CO-OX_{1-2} where X_{1-2} is C_1-C_4 alkyl or –CH_2-φ,

-CO-X_{1-2} where X_{1-2} is as defined above,

-CO-φ where –φ is substituted in the *o*-position with –CO-O-(C_1-C_4 alkyl),

-SO_2-(C_1-C_3 alkyl),

-SO_2-φ where φ is optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

–CO-OCH$_3$ and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl;

C_1-C_4 alkoxy;

-CH$_2$-OR$_{d-1}$ where R_{d-1} is –H or C_1-C_4 alkyl,

-CH$_2$-N(R$_{d-6}$)$_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R_{d-6a} where R_{d-6a} is C_1-C_4 alkyl or –φ,

-CH$_2$-O-CO-R_{d-1} where R_{d-1} is as defined above,

-CH(OR$_{d-1}$)$_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

-CH$_2$-CH$_2$-,

-CH$_2$-CH$_2$-CH$_2$-,

-CH$_2$-C(CH$_3$-)$_2$-CH$_2$-,

-CH(-O-CO-R_{d-1})$_2$ where R_{d-1} is as defined above,

-Si(R)$_3$ where R is as defined above,

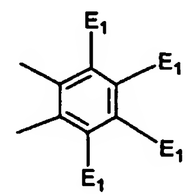
-O-Si(R)$_3$ where R is as defined above,

-Sn(R$_{b-1}$)$_3$ where R_{b-1} is as defined above,

-S-R_{d-5} where R_{d-5} is C_1-C_4 alkyl or –φ,

$-N(R_{d-6})_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

$-OE_{1-1}$ where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

$-SiE_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

$-S-E_{1-5}$ where E_{1-5} is C_1-C_4 alkyl or –φ,

$-S-(O)_{1-2}-E_{1-5}$ where E_{1-5} is as defined above,

$-N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are as defined above,

$-P(O)(O-E_{1-1})_2$ where E_{1-1} is as defined above,

$-Si(R)_3$ where R is as defined above;

$-CE_1{=}M$ (-B)

where E_1 is as defined above and

where M is:

(1) =O,

(2) $=N-E_2$ where E_2 is selected from the group consisting of

-H

C_1-C_4 alkyl,

C_1-C_4 alkenyl containing 1 or 2 double bonds,

C_1-C_4 alkynyl containing 1 triple bond,

$-CO-OE_{2-1}$ where E_{2-1} is –H or C_1-C_4 alkyl,

$-C(E_{2-1})_2-OE_{2-2}$ where E_{2-1} are the same or different and are as defined above and where E_{2-2} is

C_1-C_4 alkyl,

$-\varphi$ or

$-Si(R)_3$ where the three R are the same or different and are defined above,

$-OE_{2-2}$ where E_{2-2} is as defined above,

$-S-E_{2-3}$ where E_{2-3} is C_1-C_4 alkyl or $-\varphi$,

$-S-(O)_{1-2}-E_{2-3}$ where E_{2-3} is as defined above,

$-N(R_{d-6})_2$ where the two R_{d6} are the same or different and are as defined above;

$-Si(R)_3$ where the three R are as defined above;

(3) $=C(E_2)_2$ where the E_2 are the same or different and are as defined above,

where E_1 and E_2 are taken together with the atoms to which they are attached to form a ring of 5 thru 7 members, optionally containing 3 thru 5

$-O-$,

$-S-$,

$-N=$,

$-NX_{1-1}-$ where X_{1-1} is as defined above,

$-CE_2=$ where E_2 is as defined above,

$-C(R_b)_2-$ where R_b is as defined above, and optionally containing 1 or 2 additional double bonds;

$-C\equiv C-E_2$ (-C)

where E_2 is as defined above;

$-CH_2-CH=CH_2$ (-D1)

$-CH=C=CH_2$ (-D2)

$-CH_2-C\equiv C-H$ (-D3)

where R_9 is:

(1) $-H$,

(2) $-OH$,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of

$-Si(-CH_3)_3$,

$-Si(-CH_2-CH_3)_3$,

$-CO-CH_3$,

-CO-H and

$-SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above, and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii)) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above, with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) $-C\equiv C-H$,

(c) $-C\equiv N$,

(d) $-C\equiv C-CH_2-O-R_{17-1-1}$ where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) $-Si(R_{17-1-2})_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) $-C\equiv C-CH_2-O-$(HYDROXY PROTECTING GROUP), where HYDROXY PROTECTING GROUP is as defined above,

(f) $-CH_2-CH_2-CH_2-OH$,

(g) $-CH_2-CH_2-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) $-CH_2-CH_2-CO-O^-$ and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) $-CO-CH_3$,

(b) $-CO-CH_2-OH$,

(c) $-CO-CH_2-O-CO-(CH_2)_{0-3}-CH_3$;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing $-O-CH_2-$ where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) $-O-CH(OR_{17-9})-CH_2-CH_2\cdots\cdots$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group ($CH_2\cdots\cdots$) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH.

17. A 7α-substituted steroid (II) according to claim 16 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

18. A 7α-substituted steroid (II) according to claim 17 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

19. A 7α-substituted steroid (II) according to claim 16 where R_9 and R_{11} are selected from the group consisting of:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is

–H, and where R_{11-2} is –H.

20. A 7α-substituted steroid (II) according to claim 19 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

21. A 7α-substituted steroid (II) according to claim 16 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

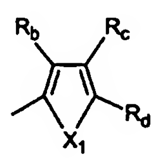
(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

22. A 7α-substituted steroid (II) according to claim 21 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

23. A 7α-substituted steroid (II) according to claim 16 where R_{7-1} is (-A1)



(-A1)

24. A 7α-substituted steroid (II) according to claim 23 where X_1 is –O-.

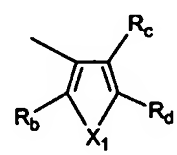
25. A 7α-substituted steroid (II) according to claim 23 where R_b and R_c are –H.

26. A 7α-substituted steroid (II) according to claim 23 where R_d is C_1 alkyl.

27. A 7α-substituted steroid (II) according to claim 23 where R_{7-1} is furan-2-yl and 5-methylfuran-2-yl.

28. A 7α-substituted steroid (II) according to claim 27 where R_{7-1} is 5-methylfuran-2-yl.

29. A 7α-substituted steroid (II) according to claim 16 where R_{7-1} is (-A2)



(-A2)

30. A 7α-substituted steroid (II) according to claim 29 where X_1 is –O-.

31. A 7α-substituted steroid (II) according to claim 29 where R_b and R_d are C_1 alkyl.

32. A 7α-substituted steroid (II) according to claim 29 where R_c is –H.

33. A 7α-substituted steroid (II) according to claim 16 where R_{7-1} is

$$-CE_2{=}M \qquad \text{(-B)}$$

34. A 7α-substituted steroid (II) according to claim 16 where R_{7-1} is

$$-C{\equiv}C\text{-}E_2 \qquad \text{(-C)}$$

35. A 7α-substituted steroid (II) according to claim 16 where R_{7-1}

$$-CH_2\text{-}CH{=}CH_2 \qquad \text{(-D1)}$$

36. A 7α-substituted steroid (II) according to claim 16 where R_{7-1}

$$-CH{=}C{=}CH_2 \qquad \text{(-D2)}$$

37. A 7α-substituted steroid (II) according to claim 16 where R_{7-1} is

$$-CH_2-C\equiv C-H \qquad (-D3)$$

38. A 7α-substituted steroid (II) according to claim 16 which is selected from the group consisting of:

17β-hydroxy-7α-(5'-methyl-2'-furyl)-pregna-4,9-dien-3-one-21-carboxylic acid, γ-lactone,

11α,17β-dihydroxy-7α-(5'-methyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone,

9α,11α-epoxy-17β-hydroxy-7α-(5'-methyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone,

17β-hydroxy-7α-(5'-t-butyl-2'-furyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone,

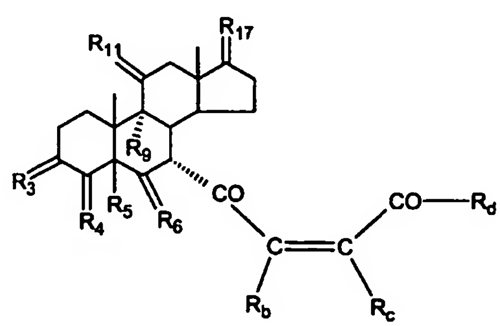
11α,17β-dihydroxy-7α-(5'-t-butyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone,

11α,17β-dihydroxy-7α-(4'-bromo-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone,

11α,17β-dihydroxy-7α-(4'-methyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone and

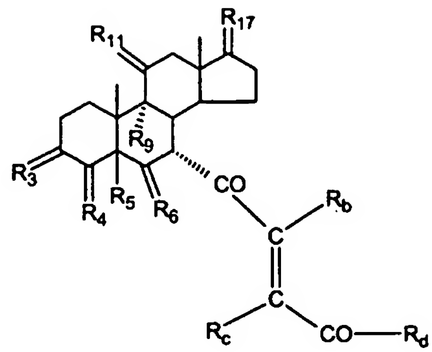
7α-allyl-17β-hydroxypregna-4,9(11)-dien-3-one, 21-carboxylic acid, γ-lactone.

39. A *cis* enedione of the formula (III-*cis*)



(III-cis)

and a trans enedione of the formula (III-*trans*)



(III-trans)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of

$-Si(-CH_3)_3$,

$-Si(-CH_2-CH_3)_3$,

$-CO-CH_3$,

-CO-H and

$-SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii)) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii)) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) $-C\equiv C-CH_2-O-R_{17-1-1}$ where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) $-Si(R_{17-1-2})_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) $-C\equiv C-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) $-CH_2-CH_2-CH_2-OH$,

(g) $-CH_2-CH_2-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) $-CH_2-CH_2-CO-O^-$ and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) $-CO-CH_3$,

(b) $-CO-CH_2-OH$,

(c) $-CO-CH_2-O-CO-(CH_2)_{0-3}-CH_3$;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing $-O-CH_2-$ where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) $-O-CH(OR_{17-9})-CH_2-CH_2\cdots\cdots$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group ($CH_2\cdots\cdots$) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12}; R_{17-10} is $-(CH_2)_{1-2}-CH=CH_2$ and R_{17-12} is –OH;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

-CO-OCH$_3$ and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl;

C_1-C_4 alkoxy;

-CH$_2$-OR_{d-1} where R_{d-1} is –H or C_1-C_4 alkyl,

-CH$_2$-N(R_{d-6})$_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R_{d-6a} where R_{d-6a} is C_1-C_4 alkyl or –φ,

-CH$_2$-O-CO-R_{d-1} where R_{d-1} is as defined above,

-CH(OR_{d-1})$_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

-CH$_2$-CH$_2$-,

-CH$_2$-CH$_2$-CH$_2$-,

-CH$_2$-C(CH$_3$-)$_2$-CH$_2$-,

-CH(-O-CO-R_{d-1})$_2$ where R_{d-1} is as defined above,

-Si(R)$_3$ where R is as defined above,

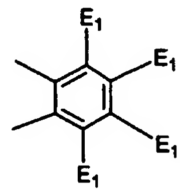
-O-Si(R)$_3$ where R is as defined above,

-Sn(R_{b-1})$_3$ where R_{b-1} is as defined above,

-S-R_{d-5} where R_{d-5} is C_1-C_4 alkyl or –φ,

-N(R_{d-6})$_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

-OE_{1-1} where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

–Si$E_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

-S-E_{1-5} where E_{1-5} is C_1-C_4 alkyl or –φ,

-S-(O)$_{1-2}$-E_{1-5} where E_{1-5} is as defined above,

-N(R_{d-6})$_2$ where the two R_{d-6} are the same or different and are as defined above,

-P(O)(O-E_{1-1})$_2$ where E_{1-1} is as defined above,

-Si(R)$_3$ where R is as defined above.

40. An enedione (III) according to claim 39 which is the cis isomer (III-cis).

41. An enedione (III) according to claim 39 which is the trans isomer (III-trans).

42. An dieneone (III) according to claim 28 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

43. An dieneone (III) according to claim 42 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

44. An dieneone (III) according to claim 28 where R_9 and R_{11} are selected from the group consisting of:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

45. An enedione (III) according to claim 44 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

46. An enedione (III) according to claim 39 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

47. An enedione (III) according to claim 46 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

48. An enedione (III) according to claim 39 where R_b and R_c are –H.

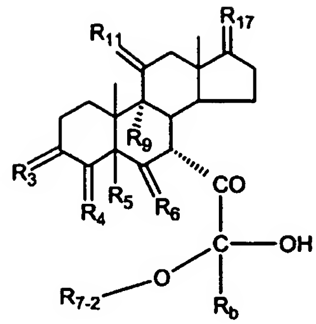
49. An enedione (III) according to claim 39 where R_d is C_1 alkyl.

50. An enedione (III) according to claim 39 which is:

17β-hydroxy-7α-(*cis*-1',4'-dioxopent-2'-en-1'yl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone,

17β-hydroxy-7α-(*trans*-1',4'-dioxopent-2'-en-1'yl)pregna-4,9-dien-3-one-21-carboxylic acid, γ-lactone.

51. A hydroxy compound of formula (IV-OH)



(IV-OH)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of

-Si(-CH_3)$_3$,

$-Si(-CH_2-CH_3)_3$,

$-CO-CH_3$,

-CO-H and

$-SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii)) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii)) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) $-C{\equiv}C\text{-}CH_2\text{-}O\text{-}R_{17\text{-}1\text{-}1}$ where $R_{17\text{-}1\text{-}1}$ is selected from the group consisting of

(i) –H,

(ii) $-Si(R_{17\text{-}1\text{-}2})_3$ where $R_{17\text{-}1\text{-}2}$ are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) $-C{\equiv}C\text{-}CH_2\text{-}O$-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) $-CH_2\text{-}CH_2\text{-}CH_2\text{-}OH$,

(g) $-CH_2\text{-}CH_2\text{-}CH_2\text{-}O$-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) $-CH_2\text{-}CH_2\text{-}CO\text{-}O^-$ and where $R_{17\text{-}2}$ is –OH;

(3) α-$R_{17\text{-}3}$:β-$R_{17\text{-}4}$ where $R_{17\text{-}3}$ is –OH and where $R_{17\text{-}4}$ is:

(a) $-CO\text{-}CH_3$,

(b) $-CO\text{-}CH_2\text{-}OH$,

(c) $-CO\text{-}CH_2\text{-}O\text{-}CO\text{-}(CH_2)_{0\text{-}3}\text{-}CH_3$;

(4) α-$R_{17\text{-}5}$:β-$R_{17\text{-}6}$ where $R_{17\text{-}5}$ and $R_{17\text{-}6}$ are taken with the attached carbon atom to form a three member epoxide containing $-O\text{-}CH_2\text{-}$ where the attachment of the –O is at $R_{17\text{-}6}$ in the β-orientation and the attachment of the CH_2- is at $R_{17\text{-}5}$ in the α-orientation;

(5) α-$R_{17\text{-}7}$:β-$R_{17\text{-}8}$ where $R_{17\text{-}7}$ and $R_{17\text{-}8}$ are taken with the attached carbon atom to form a five member lactone containing $-O\text{-}CO\text{-}CH_2\text{-}CH_2\text{-}$ where the attachment of the CH_2- is at $R_{17\text{-}7}$ in the α-orientation and the attachment of the –O is at $R_{17\text{-}8}$ in the β-orientation;

(6) $-O\text{-}CH(OR_{17\text{-}9})\text{-}CH_2\text{-}CH_2$······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where $R_{17\text{-}9}$ is –H or C_1-C_3 alkyl;

(7) α-$R_{17\text{-}11}$:β-$R_{17\text{-}12}$ where $R_{17\text{-}10}$ is $-(CH_2)_{1\text{-}2}\text{-}CH{=}CH_2$ and $R_{17\text{-}12}$ is –OH;

where R_b is selected from the group consisting of

–H,

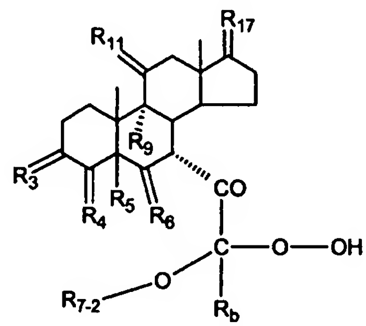
C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

where R_{7-2} is –H and C_1-C_4 alkyl optionally substituted with one or two –OH, and a hydroperoxy compound (IV-O-OH)



(IV-OOH)

where R_3, R_4, R_5, R_6, R_{7-2}, R_9, R_{11}, R_{17} and R_b are as defined above.

52. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 51 which is the hydroxy compound (IV-OH).

53. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 51 which is the hydroperoxy compound (IV-OOH).

54. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 51 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where

one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

55. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 54 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

56. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 51 where R_9 and R_{11} are selected from the group consisting of:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

57. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 56 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

58. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 51 where R_{17} is selected from the group consisting of:

(a) α-$R_{17\text{-}7}$:β-$R_{17\text{-}8}$ where $R_{17\text{-}7}$ and $R_{17\text{-}8}$ are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at $R_{17\text{-}7}$ in the α-orientation and the attachment of the –O is at $R_{17\text{-}8}$ in the β-orientation.

(b) =O;

(c) α-$R_{17\text{-}1}$:β-$R_{17\text{-}2}$ where $R_{17\text{-}1}$ is –C≡C-H and where $R_{17\text{-}2}$ is –OH;

(d) –C≡C-CH_2-O-$R_{17\text{-}1\text{-}1}$.

59. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 58 where R_{17} is:

(a) α-$R_{17\text{-}7}$:β-$R_{17\text{-}8}$ where $R_{17\text{-}7}$ and $R_{17\text{-}8}$ are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at $R_{17\text{-}7}$ in the α-orientation and the attachment of the –O is at $R_{17\text{-}8}$ in the β-orientation.

60. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 51 where R_b is –H.

61. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 51 where $R_{7\text{-}2}$ is –H, C_1 and iso-C_3.

62. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 61 where $R_{7\text{-}2}$ is –H.

63. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 61 where $R_{7\text{-}2}$ is a mixture of –H, C_1 and iso-C_3.

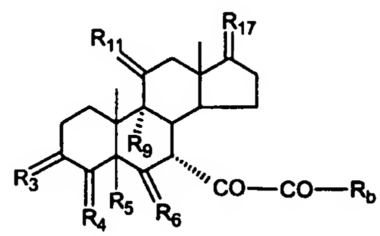
64. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 51 which is:

17β-hydroxy-7α-(1'-oxo-2'-isopropoxy-2'-hydroxyethyl)pregna-4,9-dien-3-one-21-carboxylic acid, γ-lactone,

17β-hydroxy-7α-(1'-oxo-2'-isopropoxy-2'-hydrohydroperoxy-ethyl)pregna-4,9-dien-3-one-21-carboxylic acid, γ-lactone,

17β-hydroxy-7α-(2'-hydroperoxy-2'-methoxyacetyl)pregna-4,9(11)-dien-3-one-21carboxylic acid, γ-lactone.

65. A biscarbonyl compound of the formula (V)



(V)

where:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

$-Si(-CH_3)_3$,

$-Si(-CH_2-CH_3)_3$,

$-CO-CH_3$,

-CO-H and

$-SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si(R_{17-1-2})$_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-$(CH_2)_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-$CH_2$$\cdots\cdots$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group ($CH_2$$\cdots\cdots$) is another of the four bonds at C-17 in the α-configuration

to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is –$(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy.

66. A biscarbonyl compound (V) according to claim 65 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-$(CR_{33}R_{34})_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-$(CR_{33}R_{34})_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

67. A biscarbonyl compound (V) according to claim 66 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

68. A biscarbonyl compound (V) according to claim 65 where R_9 and R_{11} are selected from the group consisting of:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

69. A biscarbonyl compound (V) according to claim 68 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

70. A biscarbonyl compound (V) according to claim 65 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

71. A biscarbonyl compound (V) according to claim 70 where R_{17} is:

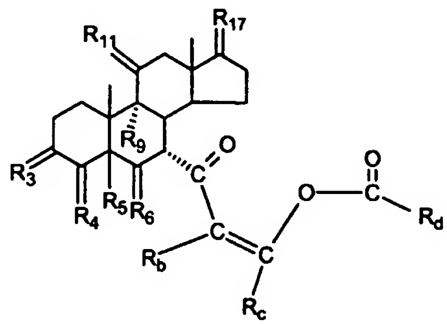
(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

72. A biscarbonyl compound (V) according to claim 65 where R_b is –H.

73. A biscarbonyl compound (V) according to claim 65 which is:

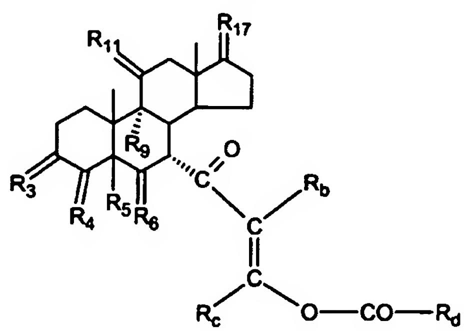
17β-hydroxy-7α-(2'-oxo-acetyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone.

74. A cis oxyenedione of the formula (X-cis)



(X-cis)

and a trans enedione of the formula (X-*trans*)



(X-trans)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is

–H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

-Si(-CH_3)$_3$,

-Si(-CH_2-CH_3)$_3$,

-CO-CH_3,

-CO-H and

-SiH(CH_3)$_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above, with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si$(R_{17-1-2})_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXYPROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-$(CH_2)_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-CH_2······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is –$(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si$(R)_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

–CO-OCH_3 and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl,

C_1-C_4 alkoxy,

-CH_2-OR_{d-1} where R_{d-1} is –H or C_1-C_4 alkyl,

-CH_2-$N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R_{d-6a} where R_{d-6a} is C_1-C_4 alkyl or –φ,

-CH_2-O-CO-R_{d-1} where R_{d-1} is as defined above,

-$CH(OR_{d-1})_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

-CH_2-CH_2-,

-CH_2-CH_2-CH_2-,

-CH_2-$C(CH_3$-$)_2$-CH_2-,

-CH(-O-CO-$R_{d-1})_2$ where R_{d-1} is as defined above,

-$Si(R)_3$ where R is as defined above,

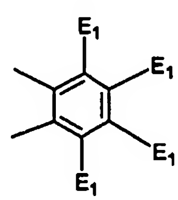
-O-$Si(R)_3$ where R is as defined above,

-$Sn(R_{b-1})_3$ where R_{b-1} is as defined above,

-S-R_{d-5} where R_{d-5} is C_1-C_4 alkyl or –φ,

-$N(R_{d-6})_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

-OE_{1-1} where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

$-SiE_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

$-S-E_{1-5}$ where E_{1-5} is C_1-C_4 alkyl or -φ,

$-S-(O)_{1-2}-E_{1-5}$ where E_{1-5} is as defined above,

$-N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are as defined above,

$-P(O)(O-E_{1-1})_2$ where E_{1-1} is as defined above,

$-Si(R)_3$ where R is as defined above.

75. An oxyenedione (X) according to claim 74 which is the cis isomer (X-cis).

76. An oxyenedione (X) according to claim 74 which is the trans isomer (X-trans).

77. An oxyenedione (X) according to claim 74 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is $-O-R_{31}$ and R_{3-6} is $-O-R_{32}$ where R_{31} and R_{32} are taken with the attached -O-C-O- to form a cyclic ketal of 5 atoms of the formula $-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$ where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is $-O-R_{31}$ and R_{3-6} is $-O-R_{32}$ where R_{31} and R_{32} are taken with the attached -O-C-O- to form a cyclic ketal of 6 atoms of the formula $-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$ where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

78. An oxyenedione (X) according to claim 65 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

79. An oxyenedione (X) according to claim 74 where R_9 and R_{11} are selected from the group consisting of:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

80. An oxyenedione (X) according to claim 79 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

81. An oxyenedione (X) according to claim 74 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

82. An oxyenedione (X) according to claim 81 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

83. An oxyenedione (X) according to claim 74 where R_b and R_c are –H.

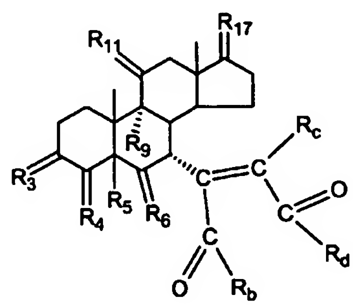
84. An oxyenedione (X) according to claim 74 where R_d is C_1 alkyl.

85. An oxyenedione (X) according to claim 74 which is:

17β-hydroxy-7α-(*cis*-3'-acetoxyacryloyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone and

17β-hydroxy-7α-(*trans*-3'-acetoxyacryloyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone.

86. A 7α-unsaturated steroid of formula (XIV)



(XIV)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is

–H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of

-Si(-CH_3)$_3$,

-Si(-CH_2-CH_3)$_3$,

-CO-CH_3,

-CO-H and

-SiH(CH_3)$_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above, with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si(R_{17-1-2})$_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-(CH_2)$_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-CH_2······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is –$(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si$(R)_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

–CO-OCH_3 and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl,

C_1-C_4 alkoxy,

-CH_2-OR_{d-1} where R_{d-1} is –H or C_1-C_4 alkyl,

-CH_2-$N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R_{d-6a} where R_{d-6a} is C_1-C_4 alkyl or –φ,

-CH_2-O-CO-R_{d-1} where R_{d-1} is as defined above,

-$CH(OR_{d-1})_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

-CH_2-CH_2-,

-CH_2-CH_2-CH_2-,

-CH_2-$C(CH_3$-$)_2$-CH_2-,

-CH(-O-CO-$R_{d-1})_2$ where R_{d-1} is as defined above,

-$Si(R)_3$ where R is as defined above,

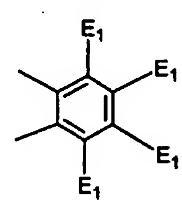
-O-$Si(R)_3$ where R is as defined above,

-$Sn(R_{b-1})_3$ where R_{b-1} is as defined above,

-S-R_{d-5} where R_{d-5} is C_1-C_4 alkyl or –φ,

-$N(R_{d-6})_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

-OE_{1-1} where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

$-SiE_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

-S-E_{1-5} where E_{1-5} is C_1-C_4 alkyl or –φ,

-S-$(O)_{1-2}$-E_{1-5} where E_{1-5} is as defined above,

-$N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are as defined above,

-P(O)(O-E_{1-1})$_2$ where E_{1-1} is as defined above,

-$Si(R)_3$ where R is as defined above.

87. A 7α-unsaturated steroid (XIV) according to claim 86 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

88. A 7α-unsaturated steroid (XIV) according to claim 87 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

89. A 7α-unsaturated steroid (XIV) according to claim 86 where R_9 and R_{11} are selected from the group consisting of:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

90. A 7α-unsaturated steroid (XIV) according to claim 89 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

91. A 7α-unsaturated steroid (XIV) according to claim 86 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

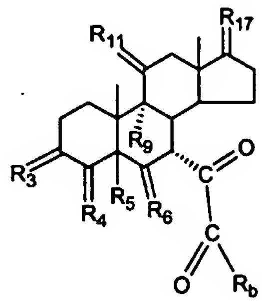
92. A 7α-unsaturated steroid (XIV) according to claim 91 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

93. A 7α-unsaturated steroid (XIV) according to claim 86 where R_b and R_c are –H.

94. A 7α-unsaturated steroid (XIV) according to claim 86 where R_d is C_1 alkyl.

95. A 7α-preacid of the formula (XV)



(XV)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

$-Si(-CH_3)_3$,

$-Si(-CH_2-CH_3)_3$,

$-CO-CH_3$,

-CO-H and

$-SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si$(R_{17-1-2})_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-$(CH_2)_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-CH_2······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration

to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is –$(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy.

96. A 7α-preacid of formula (XV) according to claim 95 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-$(CR_{33}R_{34})_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-$(CR_{33}R_{34})_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

97. A 7α-preacid of formula (XV) according to claim 96 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

98. A 7α-preacid of formula (XV) according to claim 95 where R_9 and R_{11} are selected from the group consisting of:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

99. A 7α-preacid of formula (XV) according to claim 98 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

100. A 7α-preacid of formula (XV) according to claim 95 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

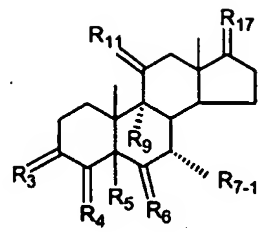
(d) –C≡C-CH_2-O-R_{17-1-1}.

101. A 7α-preacid of formula (XV) according to claim 100 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

102. A 7α-preacid of formula (XV) according to claim 95 where R_b is –H.

103. A process for the preparation of a 7α-substituted steroid (II) of the formula



(II)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(II) R_3 is R_{3-3}:R_{3-4} and R_4 is R_{4-3}:R_{4-4} where one of R_{3-3} and R_{3-4} is –O-R_{31} where R_{31} is C_1-C_3 alkyl, the other of R_{3-3} and R_{3-4} is taken together with one of R_{4-3} and R_{4-4} to form a second bond between the carbon atoms to which they are attached, and the other of R_{4-3} and R_{4-4} is –H; R_6 is R_{6-3}:R_{6-4} where one of R_{6-3} and R_{6-4} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-3} and R_{6-4} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

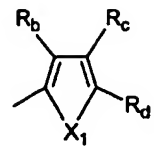
$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

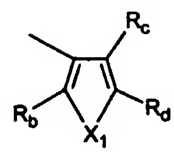
(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_{7-1} is a molecular fragment of the formula (-A1)



(-A1)

or of the formula (-A2)



(-A2)

where X_1 is:

–S-,

-O- or

–NX_{1-1}- and where X_{1-1} is:

-H,

C_1-C_4 alkyl,

-CO-OX_{1-2} where X_{1-2} is C_1-C_4 alkyl or –CH_2-φ,

-CO-X_{1-2} where X_{1-2} is as defined above,

-CO-φ where –φ is substituted in the *o*-position with –CO-O-(C_1-C_4 alkyl),

-SO_2-(C_1-C_3 alkyl),

-SO_2-φ where φ is optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

–CO-OCH_3 and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl;

C_1-C_4 alkoxy;

-CH_2-OR_{d-1} where R_{d-1} is –H or C_1-C_4 alkyl,

-CH_2-N(R_{d-6})$_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R_{d-6a} where R_{d-6a} is C_1-C_4 alkyl or –φ,

-CH_2-O-CO-R_{d-1} where R_{d-1} is as defined above,

-CH(OR_{d-1})$_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

-CH_2-CH_2-,

-CH_2-CH_2-CH_2-,

-CH_2-C(CH_3-)$_2$-CH_2-,

-CH(-O-CO-R_{d-1})$_2$ where R_{d-1} is as defined above,

-Si(R)$_3$ where R is as defined above,

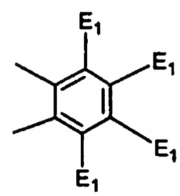
-O-Si(R)$_3$ where R is as defined above,

-Sn(R_{b-1})$_3$ where R_{b-1} is as defined above,

-S-R_{d-5} where R_{d-5} is C_1-C_4 alkyl or –φ,

-N(R_{d-6})$_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

$-OE_{1-1}$ where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

$-SiE_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

$-S-E_{1-5}$ where E_{1-5} is C_1-C_4 alkyl or –φ,

$-S-(O)_{1-2}-E_{1-5}$ where E_{1-5} is as defined above,

$-N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are as defined above,

$-P(O)(O-E_{1-1})_2$ where E_{1-1} is as defined above,

$-Si(R)_3$ where R is as defined above;

$-CE_1{=}M$ (-B)

where E_1 is as defined above and

where M is:

(1) =O,

(2) $=N-E_2$ where E_2 is selected from the group consisting of

-H

C_1-C_4 alkyl,

C_1-C_4 alkenyl containing 1 or 2 double bonds,

C_1-C_4 alkynyl containing 1 triple bond,

$-CO-OE_{2-1}$ where E_{2-1} is –H or C_1-C_4 alkyl,

$-C(E_{2-1})_2-OE_{2-2}$ where E_{2-1} are the same or different and are as defined above and where E_{2-2} is

C_1-C_4 alkyl,

$-\varphi$ or

$-Si(R)_3$ where the three R are the same or different and are defined above,

$-OE_{2-2}$ where E_{2-2} is as defined above,

$-S-E_{2-3}$ where E_{2-3} is C_1-C_4 alkyl or $-\varphi$,

$-S-(O)_{1-2}-E_{2-3}$ where E_{2-3} is as defined above,

$-N(R_{d-6})_2$ where the two R_{d6} are the same or different and are as defined above;

$-Si(R)_3$ where the three R are as defined above;

(3) $=C(E_2)_2$ where the E_2 are the same or different and are as defined above,

where E_1 and E_2 are taken together with the atoms to which they are attached to form a ring of 5 thru 7 members, optionally containing 3 thru 5

$-O-$,

$-S-$,

$-N=$,

$-NX_{1-1}-$ where X_{1-1} is as defined above,

$-CE_2=$ where E_2 is as defined above,

$-C(R_b)_2-$ where R_b is as defined above, and optionally containing 1 or 2 additional double bonds;

$-C\equiv C-E_2$ (-C)

where E_2 is as defined above;

$-CH_2-CH=CH_2$ (-D1)

$-CH=C=CH_2$ (-D2)

$-CH_2-C\equiv C-H$ (-D3)

where R_9 is:

(1) $-H$,

(2) $-OH$,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

$-Si(-CH_3)_3$,

$-Si(-CH_2-CH_3)_3$,

$-CO-CH_3$,

-CO-H and

$-SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si$(R_{17-1-2})_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-$(CH_2)_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

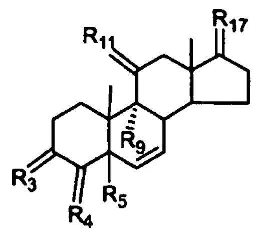
(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-CH_2······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration

to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH; which comprises:

(1) contacting a $\Delta^{4,6}$-3-keto steroid or ketal thereof (I) of the formula



(I)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached;

(I-ketal) R_3 is R_{3-9}:R_{3-10} where R_{3-9} is $-O-R_{31}$ and R_{3-10} is $-O-R_{32}$ where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

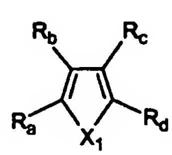
$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is R_{4-9}:R_{4-10} where one of R_{4-9} and R_{4-10} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-9} and R_{4-10} is –H;

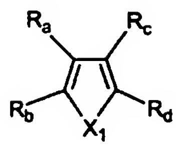
where R_9, R_{11} and R_{17} are as defined above, with an adduct selected from compounds

(a) of the formula (A)



(A1)

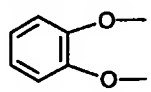
or



(A2)

where X_1, R_b, R_c and R_d are as defined above, and

where R_a is selected from the group consisting of –H, -ZnL, -BL, -SiL_3, -SnL_3, -Cu, -CuL, -AlL_2, -HgL, -Ag, -MgL, -Li and –COOH, where L is –OH, C_1-C_4 alkyl, -F, -Cl, -Br, -I, -CN, -O(C_1-C_3 alkyl), 2-thienyl, $(CH_3)_2C(O\text{-})\text{-}C(O\text{-})C(CH_3)_2$ and

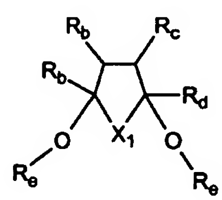
 ;

(b) of the formula (A')

$$R_b\text{-CO-CH}R_b\text{-CH}R_c\text{-CO-}R_d \qquad \text{(A')}$$

where R_b, R_c and R_d are as defined above;

(c) of the formula (A'')



(A")

where R_e is:

C_1-C_4 alkyl,

-CO-(C_1-C_4 alkyl or –φ),

-$Si(R)_3$ where R is as defined above and where X_1, R_b, R_c and R_d are as defined above;

(d) of the formula (B)

$$R_a\text{-C}E_1\text{=M} \qquad \text{(B)}$$

where R_a, E_1 and M are as defined above;

(e) of the formula (C)

$$R_a\text{-C}{\equiv}\text{C-}E_2 \qquad \text{(C)}$$

where R_a and E_2 are as defined above;

(f) of the formulas (D1, D2 and D3)

R_a-CH_2-CH=CH_2 (D1)

R_a-CH=C=CH_2 (D2)

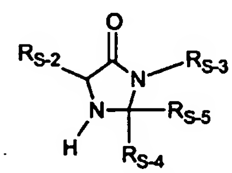
R_a-CH_2-$C\equiv C$-H (D3)

where R_a is as defined above, in the presence of:

(1) a Lewis Acid,

(2) a proton acid with a pK_a of < about 5 or

(3) a salt of a secondary amine of the formula



where:

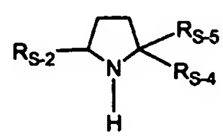
R_{S-2} is –H, C_1-C_4 alkyl, –φ, -CH_2-φ;

R_{S-3} is –H, C_1-C_4 alkyl;

R_{S-4} is –H, C_1-C_4 alkyl, –φ;

R_{S-5} is –H, C_1-C_4 alkyl, –φ;

and



where

R_{S-2} is –H, C_1-C_4 alkyl, –φ, -CH_2-φ;

R_{S-4} is –H, C_1-C_4 alkyl, –φ;

R_{S-5} is –H, C_1-C_4 alkyl, –φ;

with an acid of pK_a of < about 2.

104. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where for the 7α-substituted steroid R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

105. A process for the preparation of a 7α-substituted steroid (II) according to claim 104 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

106. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where R_9 and R_{11} are selected from the group consisting of:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

107. A process for the preparation of a 7α-substituted steroid (II) according to claim 106 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

108. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

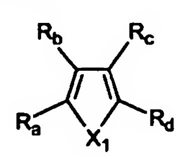
(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

109. A process for the preparation of a 7α-substituted steroid (II) according to claim 108 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

110. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where the adduct is of formula (A1)



(A1)

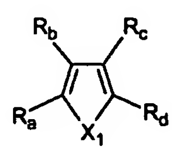
111. A process for the preparation of a 7α-substituted steroid (II) according to claim 110 where X_1 is –O-.

112. A process for the preparation of a 7α-substituted steroid (II) according to claim 110 where R_b and R_c are –H.

113. A process for the preparation of a 7α-substituted steroid (II) according to claim 110 where R_d is C_1 alkyl.

114. A process for the preparation of a 7α-substituted steroid (II) according to claim 110 where R_a is –H.

115. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where the adduct is of formula (A2)



(A2)

116. A process for the preparation of a 7α-substituted steroid (II) according to claim 115 where X_1 is –O-.

117. A process for the preparation of a 7α-substituted steroid (II) according to claim 115 where R_b and R_d are C_1 alkyl.

118. A process for the preparation of a 7α-substituted steroid (II) according to claim 115 where R_c is –H.

119. A process for the preparation of a 7α-substituted steroid (II) according to claim 115 where R_a is –H.

120. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where the adduct is (B)

$$R_a\text{-}CE_1{=}M \qquad \text{(B)}$$

121. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where the adduct is (C)

$$R_a\text{-}C{\equiv}C\text{-}E_2 \qquad (C)$$

122. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where the adduct is selected from the group consisting of (D1), (D2) and (D3)

$$R_a\text{-}CH_2\text{-}CH{=}CH_2 \qquad (D1)$$

$$R_a\text{-}CH{=}C{=}CH_2 \qquad (D2)$$

$$R_a\text{-}CH_2\text{-}C{\equiv}C\text{-}H \qquad (D3)$$

123. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where L for

-ZnL is -Cl, -Br, -I;

-BL is catecholate,

two –OH,

$HO\text{-}CH_2\text{-}CH_2\text{-}OH$,

$HO\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}OH$,

$HO\text{-}CH_2\text{-}C(CH_3)_2\text{-}CH_2\text{-}OH$;

$-SiL_3$ is C_1 alkyl;

$-SnL_3$ is C_1 or n-C_4 alkyl;

-CuL is 2-thienyl or –CN and

$-AlL_2$ is C_1-C_2 alkyl.

124. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where the process is performed in the presence of a Lewis acid.

125. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where the Lewis Acid is used in the presence of an alcohol selected from the group consisting of C_1-C_3 alcohols, ethylene glycol, 1,2- or 1,3-propylene glycol, 2,2-dimethyl- or 2,2-diethyl-1,3-propylene glycol and phenol.

126. A process for the preparation of a 7α-substituted steroid (II) according to claim 125 where the alcohol is a C_2 alcohol.

127. A process for the preparation of a 7α-substituted steroid (II) according to claim 124 where the Lewis Acid is selected from the group consisting of

BX_3, AlX_3, SnX_2, SnX_4, SiX_4, MgX_2, ZnX_2, TiX_4,
$Rh(acac)(CH_2CH_2)_2$(2,2'-bis(diphenylphosphino)-1,1'-binaphthyl),
$Rh(CH_3\text{-}C{\equiv}N)_2$(cyclooctadiene)($BF_4$),
$Rh(acac)(CH_2CH_2)_2$(dppb),
$LiClO_4$,
K10 Montmorillonite clay,
$Yb(OTf)_3$,
$LiCo(B_9C_2H_{11})_2$,
PdX_2,
CrX_3,
FeX_3,
CoX_3,
NiX_2,
SbX_5,
InX_3,
$Sc(OTf)_3$,
$\varphi_3C^+X^-$
$(R)_3SiX$ where R is C_1-C_4 alkyl and $-\varphi$;

where X is selected from the group consisting of F^-, Cl^-, Br^-, I^-, $-O-SO_2CF_3^-$, PF_6^-, BF_4^-, and ClO_4^-;

$Pd(CH_3\text{-}CO\text{-}O^-)_2$;
BF_3-diethyletherate complex;
BF_3-acetic acid complex;
BF_3-methyl-*t*-butyl ether complex;
BF_3-di-*n*-butyletherate complex;
BF_3-dimethyletherate complex;

BF_3-dimethylsulfide complex;

BF_3-phenol complex;

BF_3-phosphoric acid complex and

BF_3-tetrahydrofuran complex.

128. A process for the preparation of a 7α-substituted steroid (II) according to claim 127 where the Lewis Acid is used in the presence of an alcohol selected from the group consisting of C_1-C_3 alcohols, ethylene glycol, 1,2- or 1,3-propylene glycol, 2,2-dimethyl- or 2,2-diethyl-1,3-propylene glycol and phenol.

129. A process for the preparation of a 7α-substituted steroid (II) according to claim 127 where the Lewis Acid is selected from the group consisting of

BF_3,

BF_3-diethyletherate complex,

BF_3-acetic acid complex,

BF_3-methyl-*t*-butyl ether complex,

BF_3-di-*n*-butyletherate complex,

BF_3-dimethyletherate complex,

BF_3-dimethylsulfide complex,

BF_3-phenol complex,

BF_3-phosphoric acid complex and

BF_3-tetrahydrofuran complex.

130. A process for the preparation of a 7α-substituted steroid (II) according to claim 129 where the Lewis Acid is BF_3-diethyletherate.

131. A process for the preparation of a 7α-substituted steroid (II) according to claim 130 where the BF_3-diethyletherate is in the presence of C_1-C_3 alcohol.

132. A process for the preparation of a 7α-substituted steroid (II) according to claim 131 where the BF_3-diethyletherate is in the presence of C_2 alcohol.

133. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where the acid with a pK_a of < about 5 is selected from the group consisting of

formic acid,
acetic acid,
propionic acid,
benzoic acid,
sulfurous acid,
hydrofluoric acid,
fluoroboric acid,
p-toluenesulfonic acid,
methanesulfonic acid,
benzenesulfonic acid,
trifluoromethanesulfonic acid,
perchloric acid,
trifluoroacetic,
trichloroacetic.

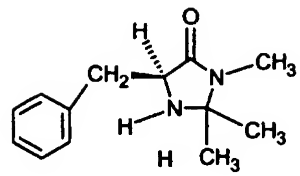
134. A process for the preparation of a 7α-substituted steroid (II) according to claim 133 where the acid is acetic acid.

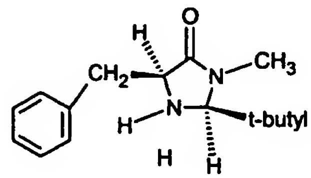
135. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where at least one equivalent of the adduct is used per equivalent of the $\Delta^{4,6}$-3-keto steroid or ketal thereof (I).

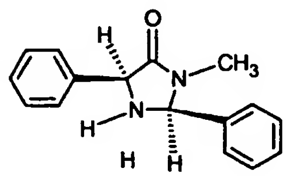
136. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where the temperature of the reaction mixture is from about -78° to about 60°.

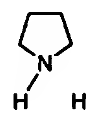
137. A process for the preparation of a 7α-substituted steroid (II) according to claim 136 where the temperature of the reaction mixture is from about -40° to about -15°.

138. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where the a salt of a secondary amine is selected from the group consisting of









and the acid with a pK_a of < about 2 is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, hydrofluoric acid, sulfuric acid, phosphoric acid , nitric acid, trichloroacetic acid and trifluoroacetic acid.

139. A process for the preparation of a 7α-substituted steroid (II) according to claim 138 where the acid of pK_a of < about 2 is hydrochloric acid.

140. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where the process is performed in a solvent/solvent mixture selected from the group consisting of:

C_1-C_6 alcohols,

a solvent mixture of C_1-C_6 alcohols and a solvent selected from the group consisting of acetonitrile, nitromethane, toluene, methylene chloride and acetic acid.

141. A process for the preparation of a 7α-substituted steroid (II) according to claim 140 where the solvent is a mixture of acetonitrile and ethanol.

142. A process for the preparation of a 7α-substituted steroid (II) according to claim 103 where the 7-substituted steroid (II) is:

17β-hydroxy-7α-(5'-methyl-2'-furyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone,

11α,17β-dihydroxy-7α-(5'-methyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone,

9α,11α-epoxy-17β-hydroxy-7α-(5'-methyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone,

17β-hydroxy-7α-(5'-t-butyl-2'-furyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone,

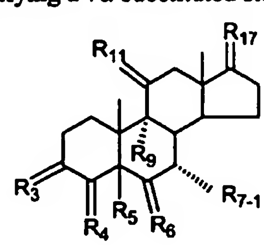
11α,17β-dihydroxy-7α-(5'-t-butyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone,

11α,17β-dihydroxy-7α-(4'-bromo-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone,

11α,17β-dihydroxy-7α-(4'-methyl-2'-furyl)-pregn-4-en-3-one-21-carboxylic acid, γ-lactone and

7α-allyl-17β-hydroxypregna-4,9(11)-dien-3-one, 21-carboxylic acid, γ-lactone.

143. A process for purifying a 7α-substituted steroid of formula (II)



(II)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(II) R_3 is R_{3-3}:R_{3-4} and R_4 is R_{4-3}:R_{4-4} where one of R_{3-3} and R_{3-4} is –O-R_{31} where R_{31} is C_1-C_3 alkyl, the other of R_{3-3} and R_{3-4} is taken together with one of R_{4-3} and R_{4-4} to form a second bond between the carbon atoms to which they are attached, and the other of R_{4-3} and R_{4-4} is –H; R_6 is R_{6-3}:R_{6-4} where one of R_{6-3} and R_{6-4} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-3} and R_{6-4} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

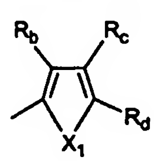
$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

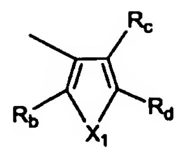
(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_{7-1} is a molecular fragment of the formula (-A1)



(-A1)

or of the formula (-A2)



(-A2)

where X_1 is:

–S-,

-O- or

–NX_{1-1}- and where X_{1-1} is:

-H,

C_1-C_4 alkyl,

-CO-OX_{1-2} where X_{1-2} is C_1-C_4 alkyl or –CH_2-φ,

-CO-X_{1-2} where X_{1-2} is as defined above,

-CO-φ where –φ is substituted in the *o*-position with –CO-O-(C_1-C_4 alkyl),

-SO_2-(C_1-C_3 alkyl),

-SO_2-φ where φ is optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

–CO-OCH_3 and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl;

C_1-C_4 alkoxy;

-CH_2-OR_{d-1} where R_{d-1} is –H or C_1-C_4 alkyl,

-CH_2-$N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R_{d-6a} where R_{d-6a} is C_1-C_4 alkyl or –φ,

-CH_2-O-CO-R_{d-1} where R_{d-1} is as defined above,

-$CH(OR_{d-1})_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

-CH_2-CH_2-,

-CH_2-CH_2-CH_2-,

-CH_2-$C(CH_3$-$)_2$-CH_2-,

-CH(-O-CO-$R_{d-1})_2$ where R_{d-1} is as defined above,

-$Si(R)_3$ where R is as defined above,

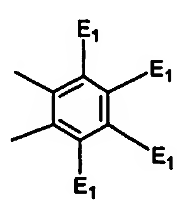
-O-$Si(R)_3$ where R is as defined above,

-$Sn(R_{b-1})_3$ where R_{b-1} is as defined above,

-S-R_{d-5} where R_{d-5} is C_1-C_4 alkyl or –φ,

-$N(R_{d-6})_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

$-OE_{1-1}$ where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

$-SiE_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

$-S-E_{1-5}$ where E_{1-5} is C_1-C_4 alkyl or –φ,

$-S-(O)_{1-2}-E_{1-5}$ where E_{1-5} is as defined above,

$-N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are as defined above,

$-P(O)(O-E_{1-1})_2$ where E_{1-1} is as defined above,

$-Si(R)_3$ where R is as defined above;

$-CE_1$=M (-B)

where E_1 is as defined above and

where M is:

(1) =O,

(2) $=N-E_2$ where E_2 is selected from the group consisting of

-H

C_1-C_4 alkyl,

C_1-C_4 alkenyl containing 1 or 2 double bonds,

C_1-C_4 alkynyl containing 1 triple bond,

$-CO-OE_{2-1}$ where E_{2-1} is –H or C_1-C_4 alkyl,

$-C(E_{2-1})_2-OE_{2-2}$ where E_{2-1} are the same or different and are as defined above and where E_{2-2} is

C_1-C_4 alkyl,

-φ or

$-Si(R)_3$ where the three R are the same or different and are defined above,

$-OE_{2-2}$ where E_{2-2} is as defined above,

$-S-E_{2-3}$ where E_{2-3} is C_1-C_4 alkyl or –φ,

$-S-(O)_{1-2}-E_{2-3}$ where E_{2-3} is as defined above,

$-N(R_{d-6})_2$ where the two R_{d6} are the same or different and are as defined above;

$-Si(R)_3$ where the three R are as defined above;

(3) $=C(E_2)_2$ where the E_2 are the same or different and are as defined above,

where E_1 and E_2 are taken together with the atoms to which they are attached to form a ring of 5 thru 7 members, optionally containing 3 thru 5

–O-,

-S-,

–N=,

$-NX_{1-1}-$ where X_{1-1} is as defined above,

$-CE_2=$ where E_2 is as defined above,

$-C(R_b)_2-$ where R_b is as defined above, and optionally containing 1 or 2 additional double bonds;

$$-C{\equiv}C-E_2 \qquad (-C)$$

where E_2 is as defined above;

$$-CH_2-CH{=}CH_2 \qquad (-D1)$$

$$-CH{=}C{=}CH_2 \qquad (-D2)$$

$$-CH_2-C{\equiv}C-H \qquad (-D3)$$

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

$-Si(-CH_3)_3$,

$-Si(-CH_2-CH_3)_3$,

$-CO-CH_3$,

-CO-H and

$-SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si(R_{17-1-2})$_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) $-C{\equiv}C-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) $-CH_2-CH_2-CH_2-OH$,

(g) $-CH_2-CH_2-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) $-CH_2-CH_2-CO-O^-$ and where $R_{17\text{-}2}$ is $-OH$;

(3) α-$R_{17\text{-}3}$:β-$R_{17\text{-}4}$ where $R_{17\text{-}3}$ is $-OH$ and where $R_{17\text{-}4}$ is:

(a) $-CO-CH_3$,

(b) $-CO-CH_2-OH$,

(c) $-CO-CH_2-O-CO-(CH_2)_{0\text{-}3}-CH_3$;

(4) α-$R_{17\text{-}5}$:β-$R_{17\text{-}6}$ where $R_{17\text{-}5}$ and $R_{17\text{-}6}$ are taken with the attached carbon atom to form a three member epoxide containing $-O-CH_2-$ where the attachment of the $-O$ is at $R_{17\text{-}6}$ in the β-orientation and the attachment of the CH_2- is at $R_{17\text{-}5}$ in the α-orientation;

(5) α-$R_{17\text{-}7}$:β-$R_{17\text{-}8}$ where $R_{17\text{-}7}$ and $R_{17\text{-}8}$ are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the CH_2- is at $R_{17\text{-}7}$ in the α-orientation and the attachment of the $-O$ is at $R_{17\text{-}8}$ in the β-orientation;

(6) $-O-CH(OR_{17\text{-}9})-CH_2-CH_2\cdots\cdots$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group ($CH_2\cdots\cdots$) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where $R_{17\text{-}9}$ is $-H$ or C_1-C_3 alkyl;

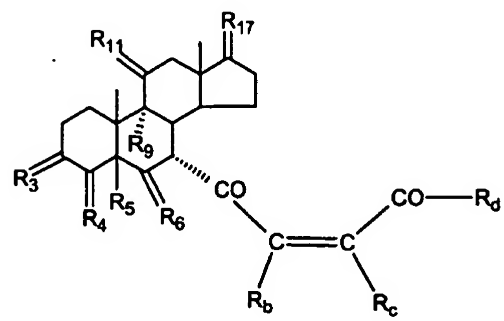
(7) α-$R_{17\text{-}11}$:β-$R_{17\text{-}12}$ where $R_{17\text{-}10}$ is $-(CH_2)_{1\text{-}2}-CH{=}CH_2$ and $R_{17\text{-}12}$ is $-OH$ to greater than 99.5% isomeric purity, which comprises:

(1) crystallizing 7α-substituted steroid (II) which contains greater than 5% of 7β-isomer from a solvent selected from the group consisting of ethyl acetate, propyl acetate and butyl acetate.

144. A process for producing a 7α-substituted steroid of formula (II) according to claim 143 where the 7α-substituted steroid (II) is obtained in greater than 99.8% isomeric purity.

145. A process for producing a 7α-substituted steroid of formula (II) according to claim 143 where the solvent is propyl acetate.

146. A process for the preparation of a *cis*-enedione of formula (III-*cis*)



(III-cis)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

-$Si(-CH_3)_3$,

-$Si(-CH_2-CH_3)_3$,

-$CO-CH_3$,

-CO-H and

-$SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si(R_{17-1-2})$_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-$(CH_2)_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) $-O-CH(OR_{17-9})-CH_2-CH_2$······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}-CH=CH_2$ and R_{17-12} is –OH;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

$-CO-OCH_3$ and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl;

C_1-C_4 alkoxy;

-CH_2-OR_{d-1} where R_{d-1} is –H or C_1-C_4 alkyl,

-CH_2-N$(R_{d-6})_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R_{d-6a} where R_{d-6a} is C_1-C_4 alkyl or –φ,

-CH_2-O-CO-R_{d-1} where R_{d-1} is as defined above,

-CH(OR_{d-1})$_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

-CH_2-CH_2-,

-CH_2-CH_2-CH_2-,

-CH_2-C(CH_3-)$_2$-CH_2-,

-CH(-O-CO-R_{d-1})$_2$ where R_{d-1} is as defined above,

-Si(R)$_3$ where R is as defined above,

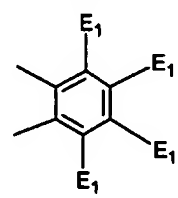
-O-Si(R)$_3$ where R is as defined above,

-Sn(R_{b-1})$_3$ where R_{b-1} is as defined above,

-S-R_{d-5} where R_{d-5} is C_1-C_4 alkyl or –φ,

-N(R_{d-6})$_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

-OE_{1-1} where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

–Si$E_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

-S-E_{1-5} where E_{1-5} is C_1-C_4 alkyl or –φ,

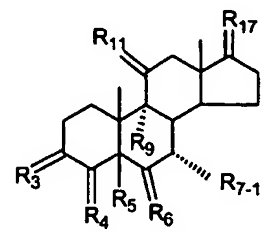
-S-(O)$_{1-2}$-E_{1-5} where E_{1-5} is as defined above,

-N(R_{d-6})$_2$ where the two R_{d-6} are the same or different and are as defined above,

-P(O)(O-E_{1-1})$_2$ where E_{1-1} is as defined above,

-Si(R)$_3$ where R is as defined above; which comprises:

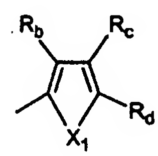
(1) contacting a 7α-substituted steroid of formula (II)



(II)

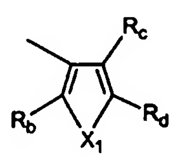
where R_3, R_4, R_5, R_6, R_9, R_{11} and R_{17} are as defined above;

where R_{7-1} is a molecular fragment of the formula (-A1)



(-A1)

or of the formula (-A2)



(-A2)

where X_1 is:

–S-,

-O- or

–NX_{1-1}- and where X_{1-1} is:

-H,

C_1-C_4 alkyl,

-CO-OX_{1-2} where X_{1-2} is C_1-C_4 alkyl or –CH_2-φ,

-CO-X_{1-2} where X_{1-2} is as defined above,

-CO-φ where –φ is substituted in the *o*-position with –CO-O-(C_1-C_4 alkyl),

-SO_2-(C_1-C_3 alkyl),

-SO_2-φ where φ is optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

where R_b, R_c and R_d are as defined above;

$-CE_1=M$ (-B)

where E_1 is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

$-OE_{1-1}$ where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

$-SiE_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

$-S-E_{1-5}$ where E_{1-5} is C_1-C_4 alkyl or –φ,

$-S-(O)_{1-2}-E_{1-5}$ where E_{1-5} is as defined above,

$-N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are as defined above,

$-P(O)(O-E_{1-1})_2$ where E_{1-1} is as defined above,

$-Si(R)_3$ where R is as defined above;

where M is:

(1) =O,

(2) $=N-E_2$ where E_2 is selected from the group consisting of:

-H

C_1-C_4 alkyl,

C_1-C_4 alkenyl containing 1 or 2 double bonds,

C_1-C_4 alkynyl containing 1 triple bond,

$-CO-OE_{2-1}$ where E_{2-1} is –H or C_1-C_4 alkyl,

$-C(E_{2-1})_2-OE_{2-2}$ where E_{2-1} are the same or different and are as defined above and where E_{2-2} is

C_1-C_4 alkyl,

-φ or

–Si(R)$_3$ where the three R are the same or different and are defined above,

-OE$_{2\text{-}2}$ where E$_{2\text{-}2}$ is as defined above,

-S-E$_{2\text{-}3}$ where E$_{2\text{-}3}$ is C$_1$-C$_4$ alkyl or –φ,

-S-(O)$_{1\text{-}2}$-E$_{2\text{-}3}$ where E$_{2\text{-}3}$ is as defined above,

-N(R$_{d\text{-}6}$)$_2$ where the two R$_{d6}$ are the same or different and are as defined above;

-Si(R)$_3$ where the three R are as defined above;

(3) =C(E$_2$)$_2$ where the E$_2$ are the same or different and are as defined above,

where E$_1$ and E$_2$ are taken together with the atoms to which they are attached to form a ring of 5 thru 7 members, optionally containing 3 thru 5

–O-,

-S-,

–N=,

-NX$_{1\text{-}1}$- where X$_{1\text{-}1}$ is as defined above,

-CE$_2$= where E$_2$ is as defined above,

-C(R$_b$)$_2$- where R$_b$ is as defined above, and optionally containing 1 or 2 additional double bonds;

-C≡C-E$_2$ (-C)

where E$_2$ is as defined above;

-CH$_2$-CH=CH$_2$ (-D1)

-CH=C=CH$_2$ (-D2)

-CH$_2$-C≡C-H (-D3)

with an agent selected from the group consisting of:

(a) a halogenating agent in the presence of water and a base whose conjugate acid has a pK$_a$ of > about 8,

(b) an oxygen donating agent,

(c) electrochemical oxidation,

(d) a quinone in the presence of water or

(e) nonquinone oxidants.

147. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 146 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

148. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 147 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

149. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 146 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

150. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 149 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

151. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 146

where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

152. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 151 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

153. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 146 where R_{7-1} is furan-2-yl and 5-methylfuran-2-yl.

154. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 153 where R_{7-1} is 5-methylfuran-2-yl.

155. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 146 where R_b and R_c are –H.

156. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 146 where R_d is C_1 alkyl.

157. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 146 where the oxygen donating agent is selected from the group consisting of:

a peracid,

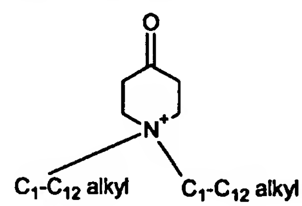
singlet oxygen followed by either phosphite or thiourea,

triplet oxygen,

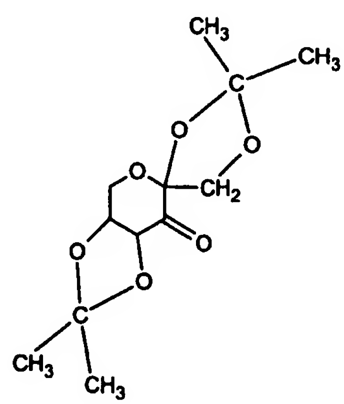
hydrogen peroxide with a ketone selected from the group consisting of Q_4-CO-Q_5 where Q_4 and Q_5 are the same or different and are

C_1-C_4 alkyl optionally substituted with 1 thru 9 –Cl or –F, and where the

Q_4 and Q_5 are taken together with the attached carbon atom to form a cyclic ketone of 5 thru 7 members and ketones of the formula:



and



hydrogen peroxide in combination with methyltrioxorhenium,

trichloroacetonitrile/hydrogen peroxide,

trichloroacetamide/hydrogen peroxide,

DDQ/water,

p-chloranil/water,

φ-$C(CH_3)_2$-O-OH or an alkylhydroperoxide in combination with a metal containing activator, where alkyl is from C_4-C_{10} alkyl and metal containing activator is selected from the group consisting of Ti(isopropoxide)$_4$, peroxotungstophosphate, VO(acetylacetonate)$_2$ and MO hexacarbonyl.

158. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 157 where the oxygen donating agent is a peracid.

159. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 158 where the peracid is selected from the group consisting of:

(a) perbenzoic acid optionally substituted with 1 or 2 –Cl or –NO_2,

(b) percarboxylic acids of the formula $C_{n2}(Q_6)2_{n2+1}$-CO_3H where n_2 is 1 thru 4 and Q_6 is –H, -Cl or –F,

(c) perphthalic acid and

(d) magnesium peroxyphthalate.

160. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 146 where the halogenating agent is selected from the group consisting of:

dibromodimethylhydantoin,

dichlorodimethylhydantoin,

diiododimethylhydantoin,

N-chlorosuccinamide,

N-bromosuccinamide,

N-iodosuccinamide,

trichloroisocyanuric acid,

t-butylhypochlorite,

3-bromo-1-chloro-5,5-dimethylhydantoin.

161. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 160 where the halogenating agent is dibromodimethylhydantoin.

162. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 146 where at least one equivalent of the halogenating agent is used.

163. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 162 where from about 1.0 to about 1.05 equivalents of the halogenating agent are used.

164. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 146 where the base is selected from the group consisting of acetate, bicarbonate, carbonate, propionate, benzoate, dibasic phosphate and borate.

165. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 164 where the base is acetate.

166. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 146 where the quinone is selected from the group consisting of DDQ, *p*-chloranil and *o*-chloranil.

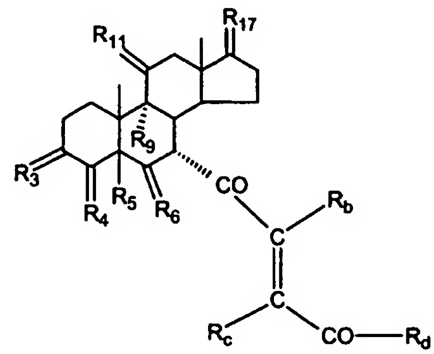
167. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 166 where the quinone is *p*-chloranil.

168. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 146 where the nonquinone oxidant is selected from the group consisting of Mn^{+3}, Mn^{+7}, Pb^{+4}, Pd^{+2}, Ru^{+8}, Cr^{+6}, ceric ammonium nitrate, iodosobenzene, iodobenzenebistrifluoroacetate, iodobenzenediacetate, tritylfluoroborate.

169. A process for the preparation of a *cis*-enedione (III-*cis*) according to claim 146 where the *cis*-enedione (III-*cis*) is:

17β-hydroxy-7α-(*cis*-1',4'-dioxopent-2'-en-1'yl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone.

170. A process for the preparation of a *trans*-enedione of formula (III-*trans*)



(III-trans)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

$-Si(-CH_3)_3$,

$-Si(-CH_2-CH_3)_3$,

$-CO-CH_3$,

-CO-H and

$-SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si$(R_{17-1-2})_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-$(CH_2)_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-CH_2······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration

to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

–CO-OCH_3 and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl;

C_1-C_4 alkoxy;

-CH_2-OR_{d-1} where R_{d-1} is –H or C_1-C_4 alkyl,

-CH_2-N(R_{d-6})$_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R_{d-6a} where R_{d-6a} is C_1-C_4 alkyl or –φ,

-CH_2-O-CO-R_{d-1} where R_{d-1} is as defined above,

$-CH(OR_{d-1})_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

$-CH_2-CH_2-$,

$-CH_2-CH_2-CH_2-$,

$-CH_2-C(CH_3-)_2-CH_2-$,

$-CH(-O-CO-R_{d-1})_2$ where R_{d-1} is as defined above,

$-Si(R)_3$ where R is as defined above,

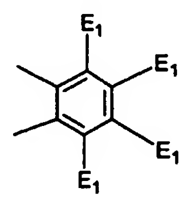
$-O-Si(R)_3$ where R is as defined above,

$-Sn(R_{b-1})_3$ where R_{b-1} is as defined above,

$-S-R_{d-5}$ where R_{d-5} is C_1-C_4 alkyl or $-\varphi$,

$-N(R_{d-6})_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

$-OE_{1-1}$ where E_{1-1} is:

-H,

C_1-C_4 alkyl,

$-\varphi$ or

$-SiE_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

$-S-E_{1-5}$ where E_{1-5} is C_1-C_4 alkyl or $-\varphi$,

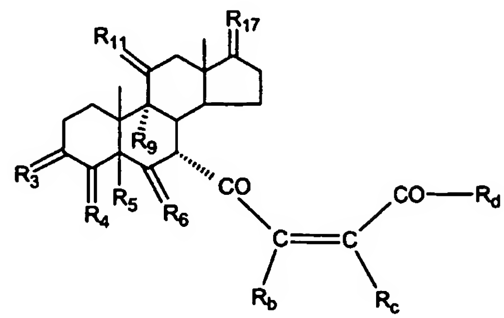
$-S-(O)_{1-2}-E_{1-5}$ where E_{1-5} is as defined above,

$-N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are as defined above,

$-P(O)(O-E_{1-1})_2$ where E_{1-1} is as defined above,

$-Si(R)_3$ where R is as defined above; which comprises:

(1) contacting a *cis*-enedione of formula (III-*cis*)



(III-cis)

where R_3, R_4, R_5, R_6, R_9, R_{11}, R_{17}, R_b, R_c and R_d are as defined above with an isomerization catalyst selected from the group consisting of:

(a) a strong acid of pK_a of < about 2;

(b) a tertiary amine whose conjugate acid has a pK_a > about 8 and

(c) salt of a tertiary amine whose conjugate acid has a pK_a > about 8,

(d) I_2,

(e) $(C_1\text{-}C_4)_3P$,

(f) φ_3P,

(g) heating to about 80°.

171. A process for the preparation of a *trans*-enedione (III-*trans*) according to claim 170 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is =O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl;

R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

172. A process for the preparation of a *trans*-enedione (III-*trans*) according to claim 171 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

173. A process for the preparation of a *trans*-enedione (III-*trans*) according to claim 170 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

174. A process for the preparation of a *trans*-enedione (III-*trans*) according to claim 173 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

175. A process for the preparation of a *trans*-enedione (III-*trans*) according to claim 170 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

176. A process for the preparation of a *trans*-enedione (III-*trans*) according to claim 175 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

177. A process for the preparation of a *trans*-enedione (III-*trans*) according to claim 170 where R_b and R_c are –H.

178. A process for the preparation of a *trans*-enedione (III-*trans*) according to claim 170 where R_d is C_1 alkyl.

179. A process for the preparation of a *trans*-enedione (III-*trans*) according to claim 170 where the isomerization catalyst is a strong acid.

180. A process for the preparation of a *trans*-enedione (III-*trans*) according to claim 179 where the strong acid is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodoic acid, hydrofluoroic acid, sulfuric acid, phosphoric acid, nitric acid, trichloroacetic acid and trifluoroacetic acid.

181. A process for the preparation of a *trans*-enedione (III-*trans*) according to claim 180 where the strong acid is hydrochloric acid.

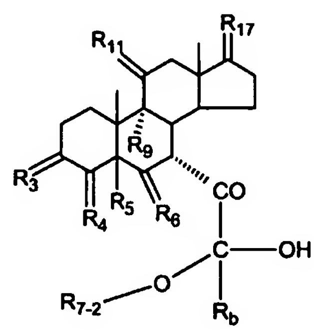
182. A process for the preparation of a *trans*-enedione (III-*trans*) according to claim 170 where the tertiary amine is selected from the group consisting of $(Q_3)_3N$ were Q_3 is C_1-C_3 alkyl, DBU, DBN, DABCO, pyridine, *p*-dimethylaminopyridine and pyrrolidinylpyridine.

183. A process for the preparation of a *trans*-enedione (III-*trans*) according to claim 182 where the tertiary amine is pyridine hydrochloride.

184. A process for the preparation of a *trans*-enedione (III-*trans*) according to claim 170 where the *trans*-enedione (III-*trans*) is:

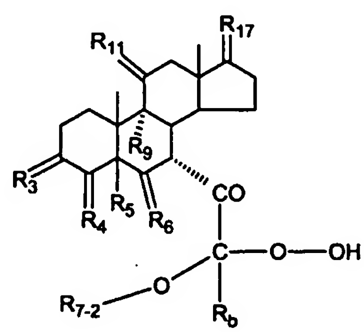
17β-hydroxy-7α-(*trans*-1',4'-dioxopent-2'-en-1'yl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone.

185. A process for the preparation of a hydroxy compound of formula (IV-OH)



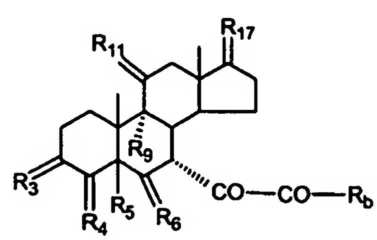
(IV-OH)

or a hydroperoxy compound of formula (IV-OOH)



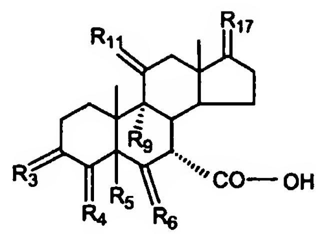
(IV-OOH)

or a biscarbonyl compound of formula (V)



(V)

or a carboxylic acid of formula (VI)



(VI)

or a mixture thereof, where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_{7-2} is –H and C_1-C_4 alkyl optionally substituted with one or two –OH,

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

-Si(-CH_3)$_3$,

-Si(-CH_2-CH_3)$_3$,

-CO-CH_3,

-CO-H and

-SiH(CH_3)$_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H, (5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH$_2$-O-R$_{17-1-1}$ where R$_{17-1-1}$ is selected from the group consisting of

(i) –H,

(ii) –Si(R$_{17-1-2}$)$_3$ where R$_{17-1-2}$ are the same or different and are C$_1$-C$_4$ alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH$_2$-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH$_2$-CH$_2$-CH$_2$-OH,

(g) –CH$_2$-CH$_2$-CH$_2$-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH$_2$-CH$_2$-CO-O$^-$ and where R$_{17-2}$ is –OH;

(3) α-R$_{17-3}$:β-R$_{17-4}$ where R$_{17-3}$ is –OH and where R$_{17-4}$ is:

(a) –CO-CH$_3$,

(b) –CO-CH$_2$-OH,

(c) –CO-CH$_2$-O-CO-(CH$_2$)$_{0-3}$-CH$_3$;

(4) α-R$_{17-5}$:β-R$_{17-6}$ where R$_{17-5}$ and R$_{17-6}$ are taken with the attached carbon atom to form a three member epoxide containing –O-CH$_2$- where the attachment of the –O is at R$_{17-6}$ in the β-orientation and the attachment of the CH$_2$- is at R$_{17-5}$ in the α-orientation;

(5) α-R$_{17-7}$:β-R$_{17-8}$ where R$_{17-7}$ and R$_{17-8}$ are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH$_2$-CH$_2$- where the attachment of the CH$_2$- is at R$_{17-7}$ in the α-orientation and the attachment of the –O is at R$_{17-8}$ in the β-orientation;

(6) –O-CH(OR$_{17-9}$)-CH$_2$-CH$_2$······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH$_2$·····) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R$_{17-9}$ is –H or C$_1$-C$_3$ alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}-CH=CH_2$ and R_{17-12} is –OH;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

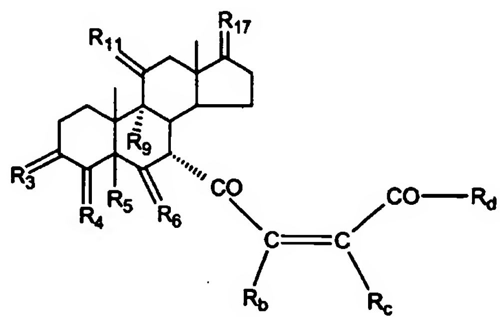
phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

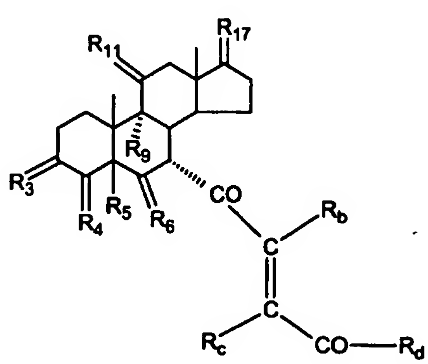
which comprises:

(1) contacting a *cis*-enedione of the formula (III-*cis*)



(III-cis)

or a *trans*-enedione of the formula (III-*trans*)



(III-trans)

or a mixture thereof,

where R_3, R_4, R_5, R_6, R_9, R_{11}, R_{17} and R_b are as defined above;

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

-CO-OCH$_3$ and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl;

C_1-C_4 alkoxy;

-CH$_2$-OR$_{d-1}$ where R_{d-1} is –H or C_1-C_4 alkyl,

-CH$_2$-N(R$_{d-6}$)$_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R_{d-6a} where R_{d-6a} is C_1-C_4 alkyl or –φ,

-CH$_2$-O-CO-R_{d-1} where R_{d-1} is as defined above,

-CH(OR$_{d-1}$)$_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

-CH$_2$-CH$_2$-,

-CH$_2$-CH$_2$-CH$_2$-,

-CH$_2$-C(CH$_3$-)$_2$-CH$_2$-,

-CH(-O-CO-R_{d-1})$_2$ where R_{d-1} is as defined above,

-Si(R)$_3$ where R is as defined above,

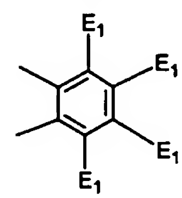
-O-Si(R)$_3$ where R is as defined above,

-Sn(R$_{b-1}$)$_3$ where R_{b-1} is as defined above,

-S-R_{d-5} where R_{d-5} is C_1-C_4 alkyl or –φ,

-N(R$_{d-6}$)$_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

-OE_{1-1} where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

–$SiE_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

-S-E_{1-5} where E_{1-5} is C_1-C_4 alkyl or –φ,

-S-$(O)_{1-2}$-E_{1-5} where E_{1-5} is as defined above,

-$N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are as defined above,

-P(O)(O-E_{1-1})$_2$ where E_{1-1} is as defined above,

-$Si(R)_3$ where R is as defined above, with ozone in the presence of an alcohol of the formula R_{7-2}-OH where R_{7-2} is as defined above.

186. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where the product is the hydroxy compound (IV-OH).

187. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where the product is the hydroperoxy compound (IV-OOH).

188. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where the product is the biscarbonyl compound (V).

189. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where the product is the carboxylic acid (VI).

190. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where the product is a mixture of two of the hydroxy compound (IV-OH), the hydroperoxy compound (IV-OOH), the biscarbonyl compound of formula (V) or the carboxylic acid (VI).

191. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 190 where the product is a mixture of the hydroxy compound (IV-OH) and the hydroperoxy compound (IV-OOH).

192. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where the product is a mixture of three of the hydroxy compound (IV-OH), the hydroperoxy compound (IV-OOH), the biscarbonyl compound (V) or the carboxylic (VI).

193. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where the product is a mixture of

the hydroxy compound (IV-OH), the hydroperoxy compound (IV-OOH) and the carboxylic acid (VI).

194. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where the product is a mixture of all four of the hydroxy compound (IV-OH), the hydroperoxy compound (IV-OOH), the biscarbonyl compound (V) and the carboxylic acid (VI).

195. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

196. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 195 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

197. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

198. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 197 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

199. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

200. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 199 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

201. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where R_b and R_c are –H.

202. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where where R_d is C_1 alkyl.

203. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 185 where R_{7-2} is –H, C_1 and iso-C_3.

204. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 203 where R_{7-2} is a mixture of –H, C_1 and iso-C_3.

205. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where the temperature of the reaction mixture is from about –100° to about 40°.

206. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 205 where the temperature of the reaction mixture is from about –78° to about –20°.

207. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 206 where the temperature of the reaction mixture is about –50°.

208. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 205 where the cooling is maintained during the ozonolysis.

209. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where the ozone is used as an ozone/oxygen mixture.

210. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where the contacting is performed by reacting the *cis*-enedione (III-*cis*) or *trans*-enedione (III-*trans*) or mixture thereof, (1) with the alcohol R_{7-2}-OH, and (2) contacting the mixture of step (1) with ozone.

211. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound (V), or a carboxylic acid (VI) or mixture thereof according to claim 185 where the products produced are:

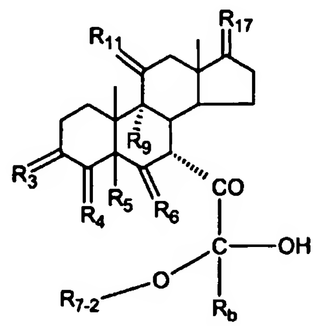
17β-hydroxy-7α-(1'-oxo-2'-isopropoxy-2'-hydroxy-ethyl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone,

17β-Hydroxy-7α-(2'-oxo-acetyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone,

17β-hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone,

17β-hydroxy-7α-(2'-hydroperoxy-2'-methoxyacetyl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone.

212. A process for the preparation of a hydroxy compound of formula (IV-OH)



(IV-OH)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_{7-2} is –H and C_1-C_4 alkyl optionally substituted with one or two –OH;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of

-Si(-CH_3)$_3$,

-Si(-CH_2-CH_3)$_3$,

-CO-CH_3,

-CO-H and

-SiH(CH_3)$_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si(R_{17-1-2})$_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-(CH_2)$_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-CH_2······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the

methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is –(CH_2)$_{1-2}$-CH=CH_2 and R_{17-12} is –OH;

where R_b is selected from the group consisting of

–H,

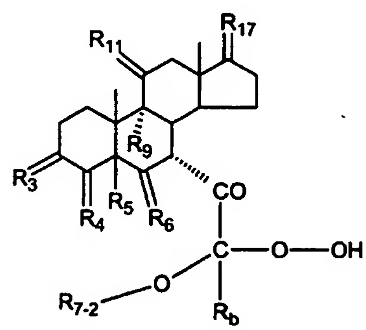
C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy; which comprises:

(1) contacting a hydroperoxy compound of formula (IV-OOH)



(IV-OOH)

where R_3, R_4, R_5, R_6, R_9, R_{11}, R_{17}, R_b and R_{7-2} are as defined above with a hydroperoxy-deoxygenating agent.

213. A process for the preparation of a hydroxy compound (IV-OH) according to claim 212 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where

one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

214. A process for the preparation of a hydroxy compound (IV-OH) according to claim 213 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

215. A process for the preparation of a hydroxy compound (IV-OH) according to claim 212 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

216. A process for the preparation of a hydroxy compound (IV-OH) according to claim 215 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

217. A process for the preparation of a hydroxy compound (IV-OH) according to claim 212 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

218. A process for the preparation of a hydroxy compound (IV-OH) according to claim 217 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

219. A process for the preparation of a hydroxy compound (IV-OH) according to claim 212 where R_b is –H.

220. A process for the preparation of a hydroxy compound (IV-OH) according to claim 212 where R_{7-2} is –H, C_1 and iso-C_3.

221. A process for the preparation of a hydroxy compound (IV-OH) according to claim 220 where R_{7-2} is a mixture of –H, C_1 and iso-C_3.

222. A process for the preparation of a hydroxy compound (IV-OH) according to claim 212 where the hydroperoxy-deoxygenating agent is selected from the group consisting of:

Q_1Q_2S where Q_1 and Q_2 are the same or different and is C_1-C_4 alkyl or phenyl,

bisulfite, sulfite, thiosulfate,

tetrahydrothiophene,

hydrosulfite,

thiourea,

butyl vinyl ether,

(C_1-C_4 alkyl)$_3$ phosphine,

triphenylphosphine, and

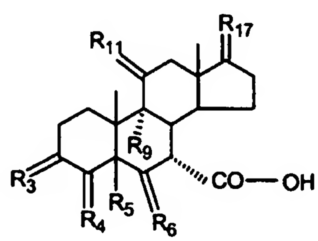
tetramethylethylene.

223. A process for the preparation of a hydroxy compound (IV-OH) according to claim 222 where Q_1 and Q_2 are both C_1 alkyl and the hydroperoxy-deoxygenating agent is dimethylsulfide.

224. A process for the preparation of a hydroxy compound (IV-OH) according to claim 212 where the hydroxy compound (IV-OH) is

17β-hydroxy-7α-(1'-oxo-2'-isopropoxy-2'-hydroxy-ethyl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone.

225. A process for the preparation of a carboxylic acid of formula (VI)



(VI)

or pharmaceutically acceptable salt thereof, where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

-Si(-CH_3)$_3$,

-Si(-CH_2-CH_3)$_3$,

-CO-CH_3,

-CO-H and

-SiH(CH_3)$_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si$(R_{17-1-2})_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-$(CH_2)_{0-3}$-CH_3;

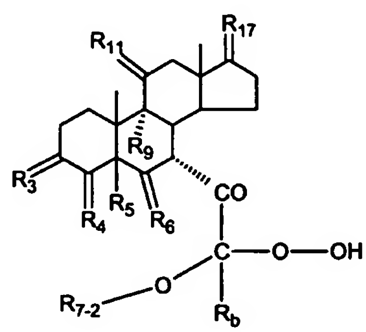
(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-CH_2······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is –$(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH; which comprises:

(1) contacting a hydroperoxy compound of formula (IV-OOH)



(IV-OOH)

where R_3, R_4, R_5, R_6, R_9, R_{11} and R_{17} are as defined above;

where R_b is where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

where R_{7-2} is –H and C_1-C_4 alkyl optionally substituted with one or two –OH; with a carboxylic acid forming agent selected from the group consisting of:

(a) heat,

(b) a base whose conjugate acid has a pK_a of about 5 or above,

(c) an acid which has a pK_a of less than about 3,

(d) an acylating agent.

226. A process for the preparation of a carboxylic acid (VI) according to claim 225 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

227. A process for the preparation of a carboxylic acid (VI) according to claim 226 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

228. A process for the preparation of a carboxylic acid (VI) according to claim 225 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

229. A process for the preparation of a carboxylic acid (VI) according to claim 228 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

230. A process for the preparation of a carboxylic acid (VI) according to claim 225 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

231. A process for the preparation of a carboxylic acid (VI) according to claim 230 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

232. A process for the preparation of a carboxylic acid (VI) according to claim 225 where R_b is –H.

233. A process for the preparation of a carboxylic acid (VI) according to claim 225 where R_{7-2} is –H, C_1 and iso-C_3.

234. A process for the preparation of a carboxylic acid (VI) according to claim 225 where R_{7-2} is –H.

235. A process for the preparation of a carboxylic acid (VI) according to claim 225 where the acid forming agent is heat.

236. A process for the preparation of a carboxylic acid (VI) according to claim 235 where the heat in the range of from about 30° to about 120°.

237. A process for the preparation of a carboxylic acid (VI) according to claim 236 where the heat is from about 80° to about 90°.

238. A process for the preparation of a carboxylic acid (VI) according to claim 225 where the acid forming agent is a base.

239. A process for the preparation of a carboxylic acid (VI) according to claim 225 where the is base is an inorganic base selected from the group consisting of hydroxide, bicarbonate, and carbonate and organic bases selected from the group consisting of $(Q_3)_3N$ were Q_3 is C_1-C_3 alkyl, DBU, DBN, DABCO, pyridine and *p*-dimethylaminopyridine.

240. A process for the preparation of a carboxylic acid (VI) according to claim 239 where the is base is bicarbonate.

241. A process for the preparation of a carboxylic acid (VI) according to claim 225 where the acid forming agent is an acid .

242. A process for the preparation of a carboxylic acid (VI) according to claim 241 where the acid is selected from the group consisting of hydrochloric acid, sulfuric

acid, phosphoric acid, nitric acid and organic acids of the formula of R_{acid-1}-COOH where R_{acid-1} is –H and C_1-C_3 alkyl optionally substituted with 1 thru 3 –Cl and -F.

243. A process for the preparation of a carboxylic acid (VI) according to claim 242 where the acid is formic acid and trifluoroacetic acid.

244. A process for the preparation of a carboxylic acid (VI) according to claim 225 where the acid forming agent is an acylating agent.

245. A process for the preparation of a carboxylic acid (VI) according to claim 244 where the acylating agent is selected from the group consisting of R_{acid-2}-CO-O-CO-R_{acid-2} where R_{acid-2} is

–H,

C_1-C_3 alkyl optionally substituted with 1 thru 3 –Cl and -F and -φ.

246. A process for the preparation of a carboxylic acid (VI) according to claim 245 where the acylating agent is acetic anhydride or trifluoracetic anhydride.

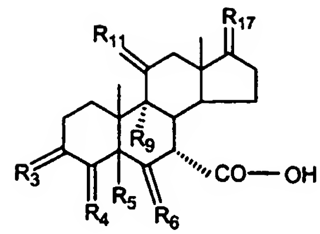
247. A process for the preparation of a carboxylic acid (VI) according to claim 225 where the acylating agent is used in the presence of an acylation catalyst.

248. A process for the preparation of a carboxylic acid (VI) according to claim 247 where the acylation catalyst is pyridine, DMAP, triethylamine and 4-pyrrolidinylpyridine.

249. A process for the preparation of a carboxylic acid (VI) according to claim 225 where the carboxylic acid (VI) is

17β-hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone.

250. A process for the preparation of a carboxylic acid of formula (VI)



(VI)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is -H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

$-Si(-CH_3)_3$,

$-Si(-CH_2-CH_3)_3$,

$-CO-CH_3$,

-CO-H and

$-SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si(R_{17-1-2})$_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-(CH_2)$_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

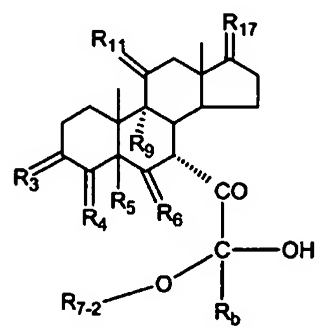
(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-CH_2······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration

to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

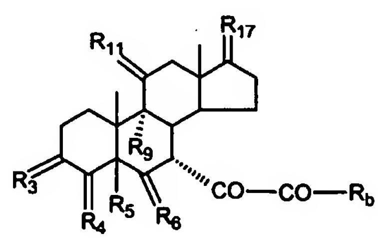
(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}$-$CH{=}CH_2$ and R_{17-12} is –OH; which comprises:

(1) contacting a hydroxy compound of formula (IV-OH)



(IV-OH)

or a biscarbonyl compound of formula (V)



(V)

or mixture thereof,

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

where R_{7-2} is –H and C_1-C_4 alkyl optionally substituted with one or two –OH; with an oxidatively cleaving agent.

251. A process for the preparation of a carboxylic acid (VI) according to claim 250 where the reactant is a hydroxy compound of formula (IV-OH).

252. A process for the preparation of a carboxylic acid (VI) according to claim 250 where the reactant is a biscarbonyl compound (V).

253. A process for the preparation of a carboxylic acid (VI) according to claim 250 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

254. A process for the preparation of a carboxylic acid (VI) according to claim 253 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

255. A process for the preparation of a carboxylic acid (VI) according to claim 250 where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

$-Si(-CH_3)_3$,

$-Si(-CH_2-CH_3)_3$,

$-CO-CH_3$,

-CO-H and

$-SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above, with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si(R_{17-1-2})$_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-(CH_2)$_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-CH_2······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration

to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is –$(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH.

256. A process for the preparation of a carboxylic acid (VI) according to claim 255 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

257. A process for the preparation of a carboxylic acid (VI) according to claim 250 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

258. A process for the preparation of a carboxylic acid (VI) according to claim 257 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

259. A process for the preparation of a carboxylic acid (VI) according to claim 250 where R_b is –H.

260. A process for the preparation of a carboxylic acid (VI) according to claim 250 where R_{7-2} is –H, C_1 and iso-C_3.

261. A process for the preparation of a carboxylic acid (VI) according to claim 260 where R_{7-2} is a mixture of –H, C_1 and iso-C_3.

262. A process for the preparation of a carboxylic acid (VI) according to claim 250 where the oxidatively cleaving agent is selected from the group consisting of:

(1) hydrogen peroxide with a carboxylic acid forming agent selected from the group consisting of:

(a) heat,

(b) a base whose conjugate acid has a pK_a of about 5 or above,

(c) an acid which has a pK_a of less than about 3,

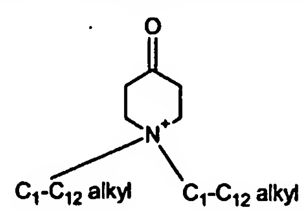
(d) an acylating agent and an acylation catalyst;

(2) $KHSO_5$;

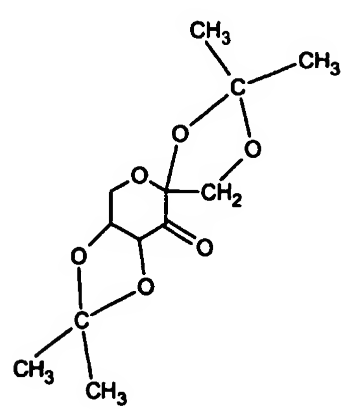
(3) hydrogen peroxide with a ketone selected from the group consisting of Q_4-CO-Q_5 where Q_4 and Q_5 are the same or different and are:

C_1-C_4 alkyl optionally substituted with 1 thru 9 –Cl or –F,

where the Q_4 and Q_5 are taken together with the attached carbon atom to form a cyclic ketone of 5 thru 7 members, and ketones of the formula:



and



(4) hydrogen peroxide in combination with methyltrioxorhenium,

(5) φ-$C(CH_3)_2$-O-OH or an alkylhydroperoxide in combination with a metal containing activator, where alkyl is from C_4-C_{10} alkyl and metal containing activator is selected from the group consisting of Ti(isopropoxide)$_4$, peroxotungstophosphate, VO(acetylacetonate)$_2$ and Mo hexacarbonyl;

(6) peracids selected from the group consisting of

(a) perbenzoic acid optionally substituted with 1 or 2 –Cl or –NO_2,

(b) percarboxylic acids of the formula $C_{n2}(Q_6)2_{n2+1}$-CO_3H where n_2 is 1 thru 4 and Q_6 is –H, -Cl or –F,

(c) perphthalic acid,

(d) magnesium peroxyphthalate.

263. A process for the preparation of a carboxylic acid (VI) according to claim 262 where the oxidatively cleaving agent is:

(1) hydrogen peroxide with a carboxylic acid forming agent.

264. A process for the preparation of a carboxylic acid (VI) according to claim 263 where the carboxylic acid forming agent is a base.

265. A process for the preparation of a carboxylic acid (VI) according to claim 264 where the is base is an inorganic base selected from the group consisting of hydroxide, bicarbonate, and carbonate and organic bases selected from the group consisting of $(Q_3)_3N$ were Q_3 is C_1-C_3 alkyl, DBU, DBN, DABCO, pyridine and *p*-dimethylaminopyridine.

266. A process for the preparation of a carboxylic acid (VI) according to claim 265 where the base is bicarbonate.

267. A process for the preparation of a carboxylic acid (VI) according to claim 263 where the carboxylic acid forming agent is an acid .

268. A process for the preparation of a carboxylic acid (VI) according to claim 267 where the acid is selected from the group consisting of hydrochloric acid, sulfuric acid, phosphoric acid, nitric acid and organic acids of the formula of R_{acid-1}-COOH where R_{acid-1} is –H and C_1-C_3 alkyl optionally substituted with 1 thru 3 –Cl and -F.

269. A process for the preparation of a carboxylic acid (VI) according to claim 268 where the acid is formic acid and trifluoroacetic acid.

270. A process for the preparation of a carboxylic acid (VI) according to claim 263 where the carboxylic acid forming agent is an acylating agent.

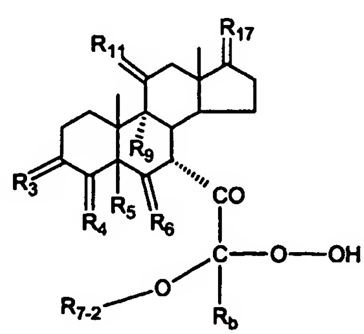
271. A process for the preparation of a carboxylic acid (VI) according to claim 270 where the acylating agent is the acylating agent is selected from the group consisting of R_{acid-2}-CO-O-CO-R_{acid-2} where R_{acid-2} is

–H,

C_1-C_3 alkyl optionally substituted with 1 thru 3 –Cl and -F and -φ.

272. A process for the preparation of a carboxylic acid (VI) according to claim 271 where the acylating agent is acetic anhydride or trifluoroacetic anhydride.

273. A process for the preparation of a carboxylic acid (VI) according to claim 250 where when the reactant is a mixture including a hydroperoxy compound of the formula (IV-OOH)



(IV-OOH)

where R_3, R_4, R_5, R_6, R_{7-2}, R_9, R_{11}, R_{17} and R_b are as defined in claim 250, the mixture is first treated with a hydroperoxy-deoxygenating agent.

274. A process for the preparation of a carboxylic acid (VI) according to claim 250 where the hydroperoxy-deoxygenating agent is selected from the group consisting of:

Q_1Q_2S where Q_1 and Q_2 are the same or different and are

C_1-C_4 alkyl,

phenyl,

bisulfite,

sulfite,

thiosulfate,

tetrahydrothiophene,

(C_1-C_4 alkyl)$_3$ phosphite,

(C_1-C_4 alkyl)$_3$ phosphine,

triphenylphosphine,

hydrosulfite,

thiourea,

butyl vinyl ether,

tetramethylethylene.

zinc and acetic acid,

tetramethylethylene and

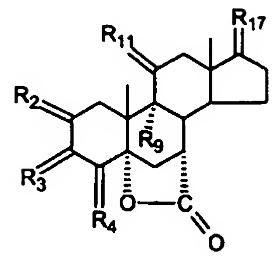
2-methylfuran.

275. A process for the preparation of a carboxylic acid (VI) according to claim 274 where the hydroperoxy-deoxygenating agent is where Q_1 and Q_2 are both C_1 alkyl and the deoxygenating agent is dimethylsulfide.

276. A process for the preparation of a carboxylic acid (VI) according to claim 250 where the carboxylic acid (VI) is:

17β-hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone.

277. A process for the preparation of a 5,7-lactone of formula (VII)



(VII)

where

(Va) R_2 is –H:-H; R_3 is = O; R_4 is –H:-H;

(Vb) R_2 is –H:-H; R_3 is R_{3a}:R_{3b} where both R_{3a} and R_{3b} are –OH and R_4 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

-Si(-CH_3)$_3$,

-Si(-CH_2-CH_3)$_3$,

-CO-CH_3,

-CO-H and

-SiH(CH_3)$_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si(R_{17-1-2})$_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-(CH_2)$_{0-3}$-CH_3;

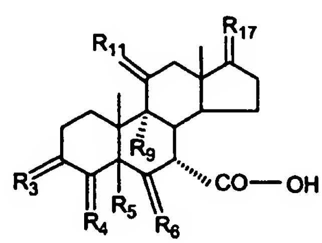
(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-CH_2⋯⋯ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2⋯⋯) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is –$(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH; which comprises:

(1) contacting a carboxylic acid of formula (VI)



(VI)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9, R_{11} and R_{17} are as defined above; with a reaction medium which has a pH of less than about 5.

278. A process for the preparation of a 5,7-lactone (VII) according to claim 277 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached.

279. A process for the preparation of a 5,7-lactone (VII) according to claim 277 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

280. A process for the preparation of a 5,7-lactone (VII) according to claim 279 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

281. A process for the preparation of a 5,7-lactone (VII) according to claim 277 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

282. A process for the preparation of a 5,7-lactone (VII) according to claim 281 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

283. A process for the preparation of a 5,7-lactone (VII) according to claim 277 where the reaction medium contains water and has a pH of from about 1 to about 5.

284. A process for the preparation of a 5,7-lactone (VII) according to claim 283 where the reaction medium contains either a strong acid of pK_a less than about 2 or a catalytic amount of base.

285. A process for the preparation of a 5,7-lactone (VII) according to claim 277 where the carboxylic acid (VI) is reacted with substantially anhydrous acid.

286. A process for the preparation of a 5,7-lactone (VII) according to claim 285 where the acid is present in an amount from catalytic to excess.

287. A process for the preparation of a 5,7-lactone (VII) according to claim 285 where the acid is selected from the group consisting of fluorosulfonic, chlorosulfonic,

benzenesulfonic, *p*-toluenesulfonic, methanesulfonic, trifluoromethanesulfonic, trifluoroacetic, trichloroacetic, hydrochloric, sulfuric, phosphoric and nitric.

288. A process for the preparation of a 5,7-lactone (VII) according to claim 287 where the acid is benzenesulfonic, *p*-toluenesulfonic or methanesulfonic.

289. A process for the preparation of a 5,7-lactone (VII) according to claim 277 where the carboxylic acid (VI) is reacted with aqueous acid in a two-phase system.

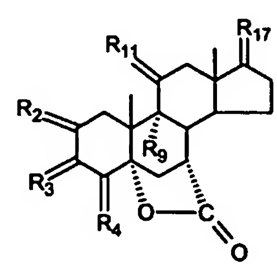
290. A process for the preparation of a 5,7-lactone (VII) according to claim 277 where the carboxylic acid (VI) is reacted with a catalytic amount of base.

291. A process for the preparation of a 5,7-lactone (VII) according to claim 292 where the base is selected from the group consisting of hydroxide, bicarbonate, carbonate, DBU, DBN, DABCO, pyridine, *p*-dimethylaminopyridine, Q_7-COO^- where Q_7 is –H, C_1-C_3 alkyl or –φ, $(Q_3)_3N$ where Q_3 is C_1-C_3 alkyl.

292. A process for the preparation of a 5,7-lactone (VII) according to claim 294 where the base is hydroxide, bicarbonate, carbonate, triethylamine or pyridine.

293. A process for the preparation of a 5,7-lactone (VII) according to claim 277 where the 5,7-lactone (VII) is obtained as a solid.

294. A process for the preparation of a 5,7-lactone of formula (VII)



(VII)

where

(Va) R_2 is –H:-H, R_3 is =O and R_4 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

$-Si(-CH_3)_3$,

$-Si(-CH_2-CH_3)_3$,

$-CO-CH_3$,

-CO-H and

$-SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si$(R_{17-1-2})_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-$(CH_2)_{0-3}$-CH_3;

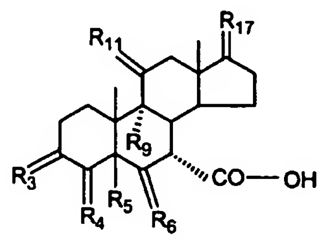
(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) $-O-CH(OR_{17-9})-CH_2-CH_2\cdots$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group ($CH_2\cdots$) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}-CH=CH_2$ and R_{17-12} is –OH; which comprises:

(1) contacting a carboxylic acid of formula (VI)



(VI)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

where R_9, R_{11} and R_{17} are as defined above; under anhydrous conditions with an anhydrous reaction medium of pH less than about 5.

295. A process for the preparation of a 5,7-lactone (VII) according to claim 294 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

296. A process for the preparation of a 5,7-lactone (VII) according to claim 294 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

297. A process for the preparation of a 5,7-lactone (VII) according to claim 294 where the reaction medium contains an acid which has a pK_a of < about 4.

298. A process for the preparation of a 5,7-lactone (VII) according to claim 294 where the acid is selected from the group consisting of fluorosulfonic, chlorosulfonic, benzenesulfonic, *p*-toluenesulfonic, methanesulfonic, trifluoromethanesulfonic, trifluoroacetic, trichloroacetic, hydrochloric, sulfuric, phosphoric and nitric.

299. A process for the preparation of a 5,7-lactone (VII) according to claim 298 where the acid is benzenesulfonic, *p*-toluenesulfonic or methanesulfonic.

300. A process for the preparation of a 5,7-lactone (VII) according to claim 294 where the carboxylic acid (VI) is reacted with the acid in a two-phase system.

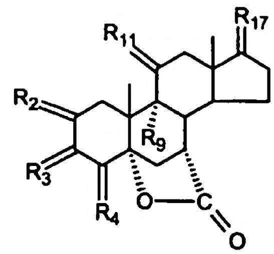
301. A process for the preparation of a 5,7-lactone (VII) according to claim 294 where the carboxylic acid (VI) is reacted with a catalytic amount of base.

302. A process for the preparation of a 5,7-lactone (VII) according to claim 294 where the base is selected from the group consisting of hydroxide, bicarbonate, carbonate, DBU, DBN, DABCO, pyridine, *p*-dimethylaminopyridine, Q_7-COO^- where Q_7 is –H, C_1-C_3 alkyl or –φ, $(Q_3)_3N$ where Q_3 is C_1-C_3 alkyl.

303. A process for the preparation of a 5,7-lactone (VII) according to claim 294 where the 5,7-lactone (VII) is obtained as a solid.

304. A process for the preparation of a 5,7-lactone (VII) according to claim 303 where the solid is crystalline.

305. A process for the preparation of a 5,7-lactone of formula (VII)



(VII)

where

(Vc) R_2 is –H:-H, R_3 is –O-R_{3a}:-O-R_{3b} where R_{3a} and R_{3b} the same and are C_1-C_3 alkyl or where R_{3a} and R_{3b} are taken together with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl, and R_4 is –H:-H;

(VI) R_2 is –H:-H; R_3 is R_{3c}:R_{3d} and R_4 is R_{4c}:R_{4d} where one of R_{3c} and R_{3d} is taken with one of R_{4c} or R_{4d} to form a second bond between the carbon atoms to which they are attached and the other of R_{3c} and R_{3d} is CH_3-O- or C_2H_5-O-; and the other of R_{4c} and R_{4d} is –H; or

(VII) R_2 is R_{2e}:R_{2f} and R_3 is R_{3e}:R_{3f} where one of R_{2e} and R_{2f} is taken with one of R_{3e} or R_{3f} to form a second bond between the carbon atoms to which they are attached and the other of R_{2e} and R_{2f} is –H, and the other of R_{3e} and R_{3f} is CH_3-O- or C_2H_5-O-; or mixtures thereof;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

-Si(-CH_3)$_3$,

-Si(-CH_2-CH_3)$_3$,

-CO-CH_3,

-CO-H and

-SiH(CH_3)$_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si(R_{17-1-2})$_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) $-C\equiv C-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) $-CH_2-CH_2-CH_2-OH$,

(g) $-CH_2-CH_2-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) $-CH_2-CH_2-CO-O^-$ and where R_{17-2} is $-OH$;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is $-OH$ and where R_{17-4} is:

(a) $-CO-CH_3$,

(b) $-CO-CH_2-OH$,

(c) $-CO-CH_2-O-CO-(CH_2)_{0-3}-CH_3$;

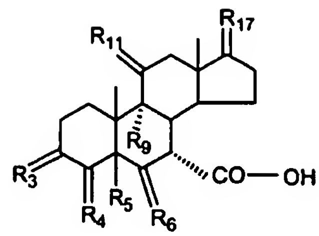
(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing $-O-CH_2-$ where the attachment of the $-O$ is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the $-O$ is at R_{17-8} in the β-orientation;

(6) $-O-CH(OR_{17-9})-CH_2-CH_2\cdots\cdots$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group ($CH_2\cdots\cdots$) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is $-H$ or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}-CH=CH_2$ and R_{17-12} is $-OH$; which comprises:

(1) contacting a carboxylic acid of formula (VI)



(VI)

where

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9, R_{11} and R_{17} are as defined above; with at least a catalytic amount of acid.

306. A process for the preparation of a 5,7-lactone (VII) according to claim 305 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

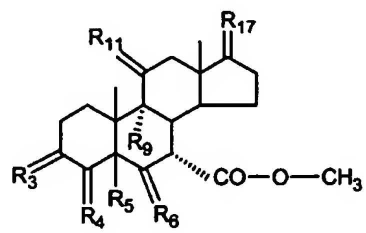
307. A process for the preparation of a 5,7-lactone (VII) according to claim 305 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

308. A process for the preparation of a 5,7-lactone (VII) according to claim 306 where the acid has a pK_a of < about 4.

309. A process for the preparation of a 5,7-lactone (VII) according to claim 305 where the 5,7-lactone (VII) is a solid.

310. A process for the preparation of a methyl ester of formula (VIII)



(VIII)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

-Si(-CH_3)$_3$,

-Si(-CH_2-CH_3)$_3$,

-CO-CH_3,

-CO-H and

-SiH(CH_3)$_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) $-Si(R_{17-1-2})_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) $-C{\equiv}C-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) $-CH_2-CH_2-CH_2-OH$,

(g) $-CH_2-CH_2-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) $-CH_2-CH_2-CO-O^{\bullet}$ and where R_{17-2} is $-OH$;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is $-OH$ and where R_{17-4} is:

(a) $-CO-CH_3$,

(b) $-CO-CH_2-OH$,

(c) $-CO-CH_2-O-CO-(CH_2)_{0-3}-CH_3$;

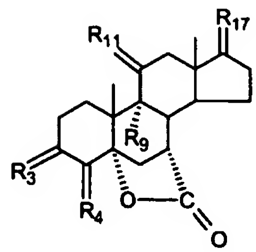
(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing $-O-CH_2-$ where the attachment of the $-O$ is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the $-O$ is at R_{17-8} in the β-orientation;

(6) $-O-CH(OR_{17-9})-CH_2-CH_2^{\cdots\cdots}$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group ($CH_2^{\cdots\cdots}$) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is $-H$ or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}-CH{=}CH_2$ and R_{17-12} is $-OH$; which comprises:

(1) contacting a 5,7-lactone of the formula (VII)



(VII)

where R_4 is –H:-H and where R_3, R_9, R_{11} and R_{17} are defined above, with aqueous base, and

(2) contacting the reaction mixture of step (1) with a methylating agent.

311. A process for the preparation of a methyl ester (VIII) according to claim 310 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

312. A process for the preparation of a methyl ester (VIII) according to claim 311 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

313. A process for the preparation of a methyl ester (VIII) according to claim 310 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the -CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) $-C \equiv C-CH_2-O-R_{17-1-1}$.

314. A process for the preparation of a methyl ester (VIII) according to claim 313 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the $-CH_2-$ is at R_{17-7} in the α-orientation and the attachment of the $-O$ is at R_{17-8} in the β-orientation.

315. A process for the preparation of a methyl ester (VIII) according to claim 310 where the amount of the methylating agent is the same as the number of equivalents of base used or a very slight excess over that.

316. A process for the preparation of a methyl ester (VIII) according to claim 310 where the methylating agent is selected from the group consisting of dimethylsulfate, methyl iodide, methyl bromide, trimethylphosphate, dimethylcarbonate and methyl chloroformate.

317. A process for the preparation of a methyl ester (VIII) according to claim 316 where the methylating agent is dimethylsulfate.

318. A process for the preparation of a methyl ester (VIII) according to claim 310 where the amount of base is from about 1 to about 1.5 equivalents.

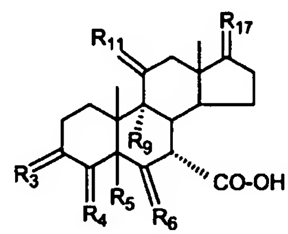
319. A process for the preparation of a methyl ester (VIII) according to claim 310 where the base is selected from the group consisting of bicarbonate, carbonate, hydroxide and $R_{base}O^-$ where R_{base} is C_1-C_4 alkyl.

320. A process for the preparation of a methyl ester (VIII) according to claim 319 where the base is bicarbonate.

321. A process for the preparation of a methyl ester (VIII) according to claim 310 where the methyl ester (VIII) is:

17β-Hydroxy-7α-carbomethoxypregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone.

322. A process for the preparation of a carboxylic acid of the formula (VI)



(VI)

or pharmaceutically acceptable salts there of, where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

-Si(-CH_3)$_3$,

-Si(-CH_2-CH_3)$_3$,

-CO-CH_3,

-CO-H and

-SiH(CH_3)$_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) $-O-R_{11-3}$ where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) $-O-R_{11-4}$ where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) $R_{11-5}:R_{11-6}$ where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O– to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) $-C{\equiv}C-CH_2-O-R_{17-1-1}$ where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) $-Si(R_{17-1-2})_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) $-C{\equiv}C-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) $-CH_2-CH_2-CH_2-OH$,

(g) $-CH_2-CH_2-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) $-CH_2-CH_2-CO-O^-$ and where R_{17-2} is $-OH$;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is $-OH$ and where R_{17-4} is:

(a) $-CO-CH_3$,

(b) $-CO-CH_2-OH$,

(c) $-CO-CH_2-O-CO-(CH_2)_{0-3}-CH_3$;

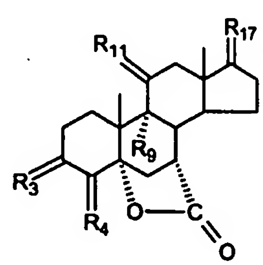
(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing $-O-CH_2-$ where the attachment of the $-O$ is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the $-O$ is at R_{17-8} in the β-orientation;

(6) $-O-CH(OR_{17-9})-CH_2-CH_2$······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is $-H$ or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}-CH=CH_2$ and R_{17-12} is $-OH$; which comprises:

(1) contacting a 5,7-lactone of formula (VII)



(VII)

where R_4 is $-H$:$-H$; and where R_3, R_9, R_{11} and R_{17} are as defined above, with a reaction medium which as a pH > 7.

323. A process for the preparation of a carboxylic acid (VI) or a pharmaceutically acceptable salts there of according to claim 322 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

324. A process for the preparation of a carboxylic acid (VI) or a pharmaceutically acceptable salts there of according to claim 323 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

325. A process for the preparation of a carboxylic acid (VI) or a pharmaceutically acceptable salts there of according to claim 322 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

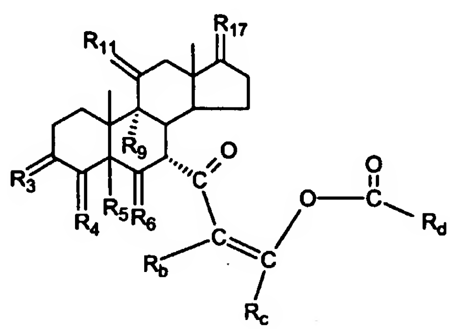
326. A process for the preparation of a carboxylic acid (VI) or a pharmaceutically acceptable salts there of according to claim 325 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the -CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

327. A process for the preparation of a carboxylic acid (VI) or a pharmaceutically acceptable salts there of according to claim 322 where the pH is kept > 7 with a base which is selected from the group consisting of bicarbonate, carbonate, hydroxide and $R_{base}O^-$ where R_{base} is C_1-C_4 alkyl.

328. A process for the preparation of a carboxylic acid (VI) or a pharmaceutically acceptable salts there of according to claim 327 where the base is bicarbonate.

329. A process for the preparation of a *cis*-oxyenedione of the formula (X-*cis*)



(X-cis)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of

R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

-Si(-CH_3)$_3$,

-Si(-CH_2-CH_3)$_3$,

-CO-CH_3,

-CO-H and

-SiH(CH_3)$_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si(R_{17-1-2})$_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-(CH_2)$_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-$CH_2$$\cdots\cdots$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group ($CH_2$$\cdots\cdots$) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is –$(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

-CO-OCH_3 and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl;

C_1-C_4 alkoxy;

-CH_2-OR_{d-1} where R_{d-1} is –H or C_1-C_4 alkyl,

$-CH_2-N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

$-\varphi$,

$-CO-R_{d-6a}$ where R_{d-6a} is C_1-C_4 alkyl or $-\varphi$,

$-CH_2-O-CO-R_{d-1}$ where R_{d-1} is as defined above,

$-CH(OR_{d-1})_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

$-CH_2-CH_2-$,

$-CH_2-CH_2-CH_2-$,

$-CH_2-C(CH_3-)_2-CH_2-$,

$-CH(-O-CO-R_{d-1})_2$ where R_{d-1} is as defined above,

$-Si(R)_3$ where R is as defined above,

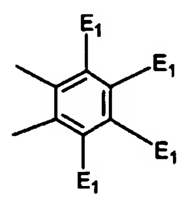
$-O-Si(R)_3$ where R is as defined above,

$-Sn(R_{b-1})_3$ where R_{b-1} is as defined above,

$-S-R_{d-5}$ where R_{d-5} is C_1-C_4 alkyl or $-\varphi$,

$-N(R_{d-6})_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

$-OE_{1-1}$ where E_{1-1} is:

-H,

C_1-C_4 alkyl,

$-\varphi$ or

$-SiE_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

$-S-E_{1-5}$ where E_{1-5} is C_1-C_4 alkyl or $-\varphi$,

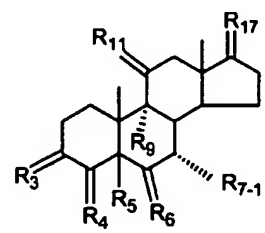
$-S-(O)_{1-2}-E_{1-5}$ where E_{1-5} is as defined above,

$-N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are as defined above,

$-P(O)(O-E_{1-1})_2$ where E_{1-1} is as defined above,

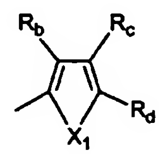
$-Si(R)_3$ where R is as defined above; which comprises:

(1) contacting a 7α-substituted steroid of formula (II)



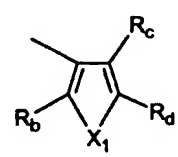
(II)

where R_{7-1} is a molecular fragment of the formula (-A1)



(-A1)

or of the formula (-A2)



(-A2)

where X_1 is:

-S-,

-O- or

$-NX_{1-1}-$ and where X_{1-1} is:

-H,

C_1-C_4 alkyl,

$-CO-OX_{1-2}$ where X_{1-2} is C_1-C_4 alkyl or $-CH_2-\varphi$,

$-CO-X_{1-2}$ where X_{1-2} is as defined above,

$-CO-\varphi$ where $-\varphi$ is substituted in the *o*-position with $-CO-O-(C_1$-C_4 alkyl),

$-SO_2-(C_1$-C_3 alkyl),

$-SO_2-\varphi$ where φ is optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

where R_b, R_c and R_d are as defined above;

$-CE_1=M$ (-B)

where E_1 is as defined above and

where M is:

(1) =O,

(2) $=N-E_2$ where E_2 is selected from the group consisting of

-H

C_1-C_4 alkyl,

C_1-C_4 alkenyl containing 1 or 2 double bonds,

C_1-C_4 alkynyl containing 1 triple bond,

$-CO-OE_{2-1}$ where E_{2-1} is –H or C_1-C_4 alkyl,

$-C(E_{2-1})_2-OE_{2-2}$ where E_{2-1} are the same or different and are as defined above and where E_{2-2} is

C_1-C_4 alkyl,

$-\varphi$ or

$-Si(R)_3$ where the three R are the same or different and are defined above,

$-OE_{2-2}$ where E_{2-2} is as defined above,

$-S-E_{2-3}$ where E_{2-3} is C_1-C_4 alkyl or $-\varphi$,

$-S-(O)_{1-2}-E_{2-3}$ where E_{2-3} is as defined above,

$-N(R_{d-6})_2$ where the two R_{d6} are the same or different and are as defined above;

$-Si(R)_3$ where the three R are as defined above;

(3) $=C(E_2)_2$ where the E_2 are the same or different and are as defined above,

where E_1 and E_2 are taken together with the atoms to which they are attached to form a ring of 5 thru 7 members, optionally containing 3 thru 5

–O-,

-S-,

–N=,

-NX_{1-1}- where X_{1-1} is as defined above,

-CE_2= where E_2 is as defined above,

-$C(R_b)_2$- where R_b is as defined above, and optionally containing 1 or 2 additional double bonds;

$$-C{\equiv}C\text{-}E_2 \qquad (\text{-C})$$

where E_2 is as defined above;

$$-CH_2\text{-}CH{=}CH_2 \qquad (\text{-D1})$$

$$-CH{=}C{=}CH_2 \qquad (\text{-D2})$$

$$-CH_2\text{-}C{\equiv}C\text{-}H \qquad (\text{-D3})$$

where R_3, R_4, R5, R6, R_9, R_{11} and R_{17} are as defined above; with ozone in the presence of a C_1-C_4 alcohol and

(2) contacting the mixture of step (1) with a hydroperoxy-deoxygenating agent.

330. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 329 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-$(CR_{33}R_{34})_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-$(CR_{33}R_{34})_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

331. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 330 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

332. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 329 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

333. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 332 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

334. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 329 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

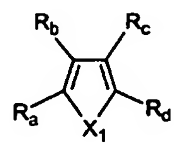
(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

335. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 334 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

336. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 329 where the adduct is of formula (A1)



(A1)

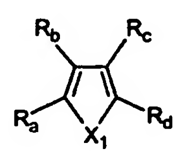
337. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 336 where X_1 is –O-.

338. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 336 where R_b and R_c are –H.

339. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 336 where R_d is C_1 alkyl.

340. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 336 where R_a is –H.

341. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 329 where the adduct is of formula (A2)



(A2)

342. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 341 where X_1 is –O-.

343. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 341 where R_b and R_d are C_1 alkyl.

344. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 341 where R_c is –H.

345. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 341 where R_a is –H.

346. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 329 where the adduct is (B)

$$R_a\text{-}CE_1\text{=}M \qquad (B)$$

347. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 329 where the adduct is (C)

$$R_a\text{-}C{\equiv}C\text{-}E_2 \qquad (C)$$

348. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 329 where the adduct is selected from the group consisting of (D1), (D2) and (D3)

$$R_a\text{-}CH_2\text{-}CH\text{=}CH_2 \qquad (D1)$$

$$R_a\text{-}CH\text{=}C\text{=}CH_2 \qquad (D2)$$

$$R_a\text{-}CH_2\text{-}C{\equiv}C\text{-}H \qquad (D3)$$

349. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 329 where the hydroperoxy-deoxygenating agent is selected from the group consisting of:

Q_1Q_2S where Q_1 and Q_2 are the same or different and are

C_1-C_4 alkyl,

phenyl,

bisulfite,

sulfite,

thiosulfate,
tetrahydrothiophene,
$(C_1\text{-}C_4 \text{ alkyl})_3$ phosphite,
$(C_1\text{-}C_4 \text{ alkyl})_3$ phosphine,
triphenylphosphine,
hydrosulfite,
thiourea,
butyl vinyl ether,
tetramethylethylene.
zinc and acetic acid,
tetramethylethylene and
2-methylfuran.

350. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 349 where the hydroperoxy-deoxygenating agent is selected from the group consisting of trimethylphosphite, tributylphosphite, triphenylphosphine and tributylphosphine.

351. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 350 where the hydroperoxy-deoxygenating agent is trimethylphosphite.

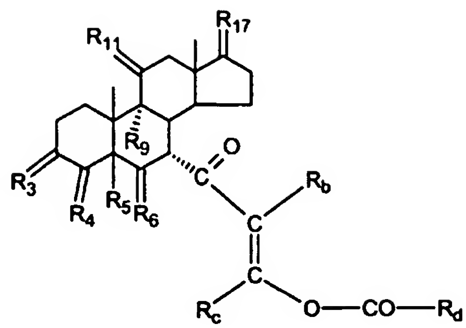
352. A process for the preparation of a *cis*-oxyenedione (X-*cis*) according to claim 329 where the alcohol is C_1 and C_3 alcohols.

353. A process for the preparation of a cis-oxyenedione (X-cis) according to claim 352 where the alcohol is a C_1 alcohol.

354. A process for the preparation of a cis-oxyenedione (X-cis) according to claim 329 where the cis-oxyenedione (X-cis) is:

17β-hydroxy-7α-(*cis*-3'-acetoxyacryloyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone.

355. A process for the preparation of a *trans*-oxyenedione of the formula (X-*trans*)



(X-trans)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of

-Si(-CH_3)$_3$,

$-Si(-CH_2-CH_3)_3$,

$-CO-CH_3$,

-CO-H and

$-SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) $-C\equiv C-CH_2-O-R_{17-1-1}$ where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) $-Si(R_{17-1-2})_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) $-C\equiv C-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) $-CH_2-CH_2-CH_2-OH$,

(g) $-CH_2-CH_2-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) $-CH_2-CH_2-CO-O^-$ and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) $-CO-CH_3$,

(b) $-CO-CH_2-OH$,

(c) $-CO-CH_2-O-CO-(CH_2)_{0-3}-CH_3$;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing $-O-CH_2-$ where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) $-O-CH(OR_{17-9})-CH_2-CH_2\cdots\cdots$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group ($CH_2\cdots\cdots$) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}-CH=CH_2$ and R_{17-12} is –OH;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

-CO-OCH$_3$ and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl;

C_1-C_4 alkoxy;

-CH$_2$-OR_{d-1} where R_{d-1} is –H or C_1-C_4 alkyl,

-CH$_2$-N(R_{d-6})$_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R_{d-6a} where R_{d-6a} is C_1-C_4 alkyl or –φ,

-CH$_2$-O-CO-R_{d-1} where R_{d-1} is as defined above,

-CH(OR_{d-1})$_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

-CH$_2$-CH$_2$-,

-CH$_2$-CH$_2$-CH$_2$-,

-CH$_2$-C(CH$_3$-)$_2$-CH$_2$-,

-CH(-O-CO-R_{d-1})$_2$ where R_{d-1} is as defined above,

-$Si(R)_3$ where R is as defined above,

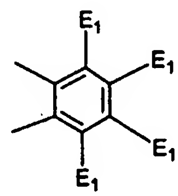
-$O-Si(R)_3$ where R is as defined above,

-$Sn(R_{b-1})_3$ where R_{b-1} is as defined above,

-$S-R_{d-5}$ where R_{d-5} is C_1-C_4 alkyl or –φ,

-$N(R_{d-6})_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

-OE_{1-1} where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

–$SiE_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

-$S-E_{1-5}$ where E_{1-5} is C_1-C_4 alkyl or –φ,

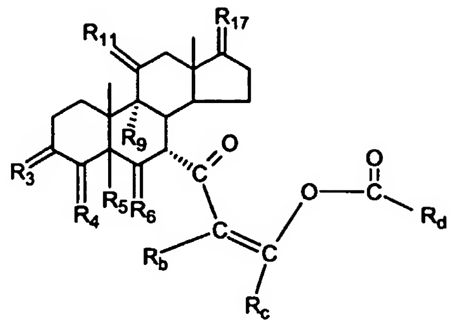
-$S-(O)_{1-2}-E_{1-5}$ where E_{1-5} is as defined above,

-$N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are as defined above,

-$P(O)(O-E_{1-1})_2$ where E_{1-1} is as defined above,

-$Si(R)_3$ where R is as defined above; which comprises:

(1) contacting a *cis*-oxyenedione of the formula (X-*cis*)



(X-cis)

where R_3, R_4, R_5, R_6, R_9, R_{11}, R_{17}, R_b, R_c and R_d are as defined above, with an isomerization catalyst selected from the group consisting of:

(a) a strong acid of pK_a of < about 2;

(b) a tertiary amine whose conjugate acid has a pK_a > about 8 and

(c) salt of a tertiary amine whose conjugate acid has a pK_a > about 8,

(d) I_2,

(e) $(C_1\text{-}C_4)_3P$,

(f) φ_3P,

(e) heating to about 80°.

356. A process for the preparation of a *trans*-oxyenedione (X-*trans*) according to claim 355 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is $R_{4\text{-}1}$:$R_{4\text{-}2}$ where one of $R_{4\text{-}1}$ and $R_{4\text{-}2}$ is –H and the other of $R_{4\text{-}1}$ and $R_{4\text{-}2}$ is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-$R_{3\text{-}5}$:β-$R_{3\text{-}6}$ where $R_{3\text{-}5}$ is –O-R_{31} and $R_{3\text{-}6}$ is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-$(CR_{33}R_{34})_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is $R_{6\text{-}5}$:$R_{6\text{-}6}$ where one of $R_{6\text{-}5}$ and $R_{6\text{-}6}$ is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of $R_{6\text{-}5}$ and $R_{6\text{-}6}$ is –H;

(III) R_3 is α-$R_{3\text{-}5}$:β-$R_{3\text{-}6}$ where $R_{3\text{-}5}$ is –O-R_{31} and $R_{3\text{-}6}$ is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-$(CR_{33}R_{34})_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is $R_{6\text{-}5}$:$R_{6\text{-}6}$ where one of $R_{6\text{-}5}$ and $R_{6\text{-}6}$ is taken together with R_5 to

form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

357. A process for the preparation of a *trans*-oxyenedione (X-*trans*) according to claim 356 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

358. A process for the preparation of a *trans*-oxyenedione (X-*trans*) according to claim 355 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

359. A process for the preparation of a *trans*-oxyenedione (X-*trans*) according to claim 358 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

360. A process for the preparation of a *trans*-oxyenedione (X-*trans*) according to claim 355 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

361. A process for the preparation of a *trans*-oxyenedione (X-*trans*) according to claim 360 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

362. A process for the preparation of a *trans*-oxyenedione (X-*trans*) according to claim 355 where R_b and R_c are –H.

363. A process for the preparation of a *trans*-oxyenedione (X-*trans*) according to claim 355 where R_d is C_1 alkyl.

364. A process for the preparation of a *trans*-oxyenedione (X-*trans*) according to claim 355 where the isomerization catalyst is a strong acid.

365. A process for the preparation of a *trans*-oxyenedione (X-*trans*) according to claim 354 where the strong acid is selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodoic acid, hydrofluoroic acid, sulfuric acid, phosphoric acid, nitric acid, trichloroacetic acid and trifluoroacetic acid.

366. A process for the preparation of a *trans*-oxyenedione (X-*trans*) according to claim 365 where the strong acid is hydrochloric acid.

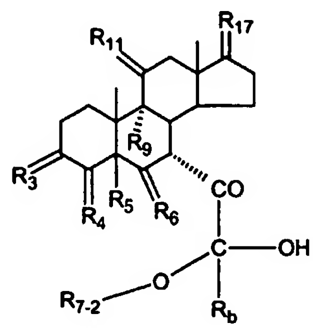
367. A process for the preparation of a *trans*-oxyenedione (X-*trans*) according to claim 355 where the tertiary amine is selected from the group consisting of $(Q_3)_3N$ were Q_3 is C_1-C_3 alkyl, DBU, DBN, DABCO, pyridine, *p*-dimethylaminopyridine and pyrrolidinylpyridine.

368. A process for the preparation of a *trans*-oxyenedione (X-*trans*) according to claim 367 where the tertiary amine is pyridine hydrochloride.

369. A process for the preparation of a *trans*-oxyenedione (X-*trans*) according to claim 355 where the *trans*-oxyenedione (X-*trans*) is

17β-hydroxy-7α-(*trans*-3'-acetoxyacryloyl)-pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone.

370. A process for the preparation of a hydroxy compound of formula (IV-OH)



(IV-OH)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken

together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

-$Si(-CH_3)_3$,

-$Si(-CH_2-CH_3)_3$,

-$CO-CH_3$,

-CO-H and

-$SiH(CH_3)_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si(R_{17-1-2})$_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-(CH_2)$_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the

attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-CH_2····· where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is –$(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH;

where R_b is selected from the group consisting of

–H,

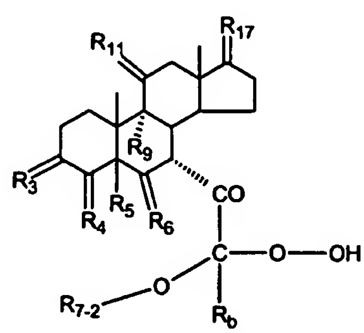
C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

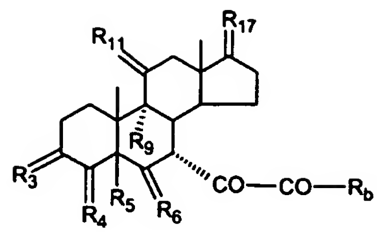
C_1-C_4 alkoxy;

where R_{7-2} is –H and C_1-C_4 alkyl optionally substituted with one or two –OH, or a hydroperoxy compound of formula (IV-OOH)



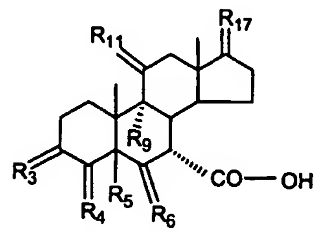
(IV-OOH)

where R_3, R_4, R_5, R_6, R_{7-2}, R_9, R_{11}, R_{17} and R_b are as defined above, or a biscarbonyl compound of formula (V)



(V)

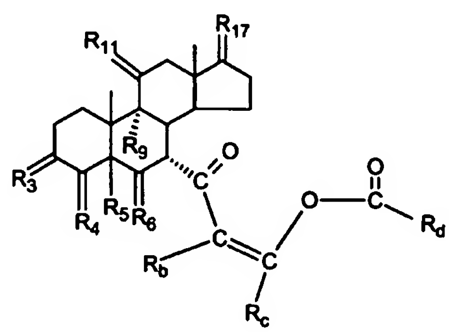
where R_3, R_4, R_5, R_6, R_9, R_{11}, R_{17} and R_b are as defined above, or a carboxylic acid of formula (VI)



(VI)

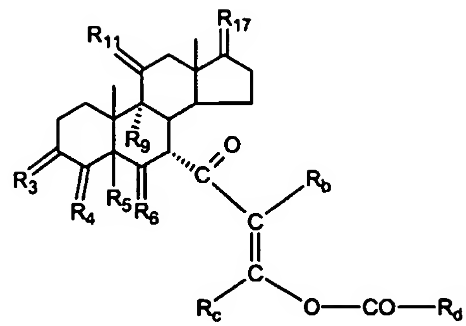
where R_3, R_4, R_5, R_6, R_9, R_{11} and R_{17} are as defined above, or a mixture thereof, which comprises:

(1) contacting an oxyenedione of the formula (X-*cis*)



(X-cis)

where R_3, R_4, R_5, R_6, R_9, R_{11}, R_{17}, R_b, R_c and R_d are as defined above or an oxyenedione of the formula (X-*trans*)



(X-trans)

where R_3, R_4, R_5, R_6, R_9, R_{11}, R_{17}, R_b, R_c and R_d are as defined above or mixture there of, with:

ozone in the presence of an alcohol of the formula $R_{7\text{-}2}$-OH where $R_{7\text{-}2}$ is as defined above.

371. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic (VI) or mixture thereof according to claim 370 where the product is the hydroxy compound (IV-OH).

372. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic (VI) or mixture thereof according to claim 370 where the product is the hydroperoxy compound (IV-OOH).

373. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic (VI) or mixture thereof according to claim 370 where the product is the biscarbonyl compound (V).

374. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic (VI) or mixture thereof according to claim 370 where the product is the carboxylic acid (VI).

375. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic (VI) or mixture thereof according to claim 370 where the product is a mixture of two of the hydroxy compound (IV-OH), the hydroperoxy compound (IV-OOH), the biscarbonyl compound of formula (V) or the carboxylic (VI).

376. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 375 where the product is a mixture of the hydroxy compound (IV-OH) and the hydroperoxy compound (IV-OOH).

377. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 370 where the product is a mixture of three of the hydroxy compound (IV-OH), the hydroperoxy compound (IV-OOH), the biscarbonyl compound of formula (V) or the carboxylic (VI).

378. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 377 where the product is a mixture of the hydroxy compound (IV-OH), the hydroperoxy compound (IV-OOH) and the carboxylic (VI).

379. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 370 where the product is a mixture of all four of the hydroxy compound (IV-OH), the hydroperoxy compound (IV-OOH), the biscarbonyl compound of formula (V) and the carboxylic (VI).

380. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 370 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is $= O$; R_4 is $R_{4-1}:R_{4-2}$ where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula $-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$ where n_1 is 0; R_4 is –H:-H; R_6 is $R_{6-5}:R_{6-6}$ where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula $-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$ where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is $R_{6-5}:R_{6-6}$ where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

381. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 380 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is $= O$; R_4 is $R_{4-1}:R_{4-2}$ where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

382. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 370 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

383. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 382 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

384. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 370 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

385. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 384 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the

attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

386. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 370 where R_b and R_c are –H.

387. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 370 where R_d is C_1 alkyl.

388. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 370 where R_{7-2} is –H, C_1 and iso-C_3.

389. A hydroxy compound (IV-OH) or hydroperoxy compound (IV-OOH) according to claim 388 where R_{7-2} is a mixture of –H, C_1 and iso-C_3.

390. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 370 where the reaction mixture is cooled to about 0°.

391. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 390 where the reaction mixture is cooled to about –100° to about –10°.

392. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a

carboxylic of formula (VI) or mixture thereof according to claim 391 where the reaction mixture is cooled to about –78° to about –20°.

393. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 392 where the reaction mixture is cooled to about –50°.

394. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 390 where the cooling is maintained during step (2).

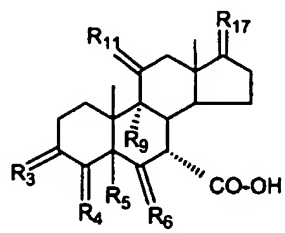
395. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 370 where the ozone is used as an ozone/oxygen mixture.

396. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 370 where the contacting is performed by reacting the *cis*-oxyenedione (X-*cis*) or *trans*-oxyenedione (X-*trans*) or mixture there of, (1) with the alcohol $R_{7\text{-}2}$-OH, and (2) contacting the mixture of step (1) with ozone.

397. A process for the preparation of a hydroxy compound (IV-OH), or a hydroperoxy compound (IV-OOH), or a biscarbonyl compound of formula (V), or a carboxylic of formula (VI) or mixture thereof according to claim 370 where the products produced is

17β-hydroxy-7α-(2'-hydroperoxy-2'-methoxyacetyl)pregna-4,9(11)-dien-3-one-21-carboxylic acid, γ-lactone.

398. A process to prepare a carboxylic acid of formula (VI)



(VI)

or salt thereof where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

$-Si(-CH_3)_3$,

-Si(-CH_2-CH_3)$_3$,

-CO-CH_3,

-CO-H and

-SiH(CH_3)$_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) $-C\equiv C-CH_2-O-R_{17-1-1}$ where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) $-Si(R_{17-1-2})_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) $-C\equiv C-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) $-CH_2-CH_2-CH_2-OH$,

(g) $-CH_2-CH_2-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) $-CH_2-CH_2-CO-O^-$ and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) $-CO-CH_3$,

(b) $-CO-CH_2-OH$,

(c) $-CO-CH_2-O-CO-(CH_2)_{0-3}-CH_3$;

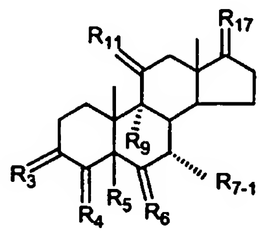
(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing $-O-CH_2-$ where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) $-O-CH(OR_{17-9})-CH_2-CH_2^{\cdots\cdots}$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group ($CH_2^{\cdots\cdots}$) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

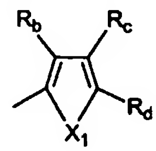
(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}-CH=CH_2$ and R_{17-12} is –OH which comprises:

(1) contacting a 7α-substituted steroid of formula (II)



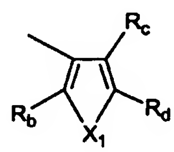
(II)

where R_{7-1} is a molecular fragment of the formula (-A1)



(-A1)

or of the formula (-A2)



(-A2)

where X_1 is:

–S-,

-O- or

–NX_{1-1}- and where X_{1-1} is:

-H,

C_1-C_4 alkyl,

-CO-OX_{1-2} where X_{1-2} is C_1-C_4 alkyl or –CH_2-φ,

-CO-X_{1-2} where X_{1-2} is as defined above,

-CO-φ where –φ is substituted in the *o*-position with –CO-O-(C_1-C_4 alkyl),

-SO_2-(C_1-C_3 alkyl),

-SO_2-φ where φ is optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

–CO-OCH$_3$ and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl;

C_1-C_4 alkoxy;

-CH$_2$-OR$_{d-1}$ where R_{d-1} is –H or C_1-C_4 alkyl,

-CH$_2$-N(R$_{d-6}$)$_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R_{d-6a} where R_{d-6a} is C_1-C_4 alkyl or –φ,

-CH$_2$-O-CO-R_{d-1} where R_{d-1} is as defined above,

-CH(OR$_{d-1}$)$_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

-CH$_2$-CH$_2$-,

-CH$_2$-CH$_2$-CH$_2$-,

-CH$_2$-C(CH$_3$-)$_2$-CH$_2$-,

-CH(-O-CO-R_{d-1})$_2$ where R_{d-1} is as defined above,

-Si(R)$_3$ where R is as defined above,

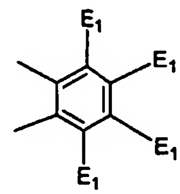
-O-Si(R)$_3$ where R is as defined above,

-Sn(R$_{b-1}$)$_3$ where R$_{b-1}$ is as defined above,

-S-R$_{d-5}$ where R$_{d-5}$ is C_1-C_4 alkyl or –φ,

-N(R$_{d-6}$)$_2$ where R$_{d-6}$ is as defined above,

where R$_c$ and R$_d$ taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

-OE$_{1-1}$ where E$_{1-1}$ is:

-H,

C_1-C_4 alkyl,

-φ or

–SiE$_{1-2}$E$_{1-3}$E$_{1-4}$ where E$_{1-2}$, E$_{1-3}$ and E$_{1-4}$ are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

-S-E$_{1-5}$ where E$_{1-5}$ is C_1-C_4 alkyl or –φ,

-S-(O)$_{1-2}$-E$_{1-5}$ where E$_{1-5}$ is as defined above,

-N(R$_{d-6}$)$_2$ where the two R$_{d-6}$ are the same or different and are as defined above,

-P(O)(O-E$_{1-1}$)$_2$ where E$_{1-1}$ is as defined above,

-Si(R)$_3$ where R is as defined above;

-CE$_1$=M (-B)

where E_1 is as defined above and

where M is:

(1) =O,

(2) =N-E$_2$ where E$_2$ is selected from the group consisting of

-H

C_1-C_4 alkyl,

C_1-C_4 alkenyl containing 1 or 2 double bonds,

C_1-C_4 alkynyl containing 1 triple bond,

-CO-OE_{2-1} where E_{2-1} is –H or C_1-C_4 alkyl,

-C(E_{2-1})$_2$-OE_{2-2} where E_{2-1} are the same or different and are as defined above and where E_{2-2} is

C_1-C_4 alkyl,

-φ or

–Si(R)$_3$ where the three R are the same or different and are defined above,

-OE_{2-2} where E_{2-2} is as defined above,

-S-E_{2-3} where E_{2-3} is C_1-C_4 alkyl or –φ,

-S-(O)$_{1-2}$-E_{2-3} where E_{2-3} is as defined above,

-N(R_{d-6})$_2$ where the two R_{d6} are the same or different and are as defined above;

-Si(R)$_3$ where the three R are as defined above;

(3) =C(E_2)$_2$ where the E_2 are the same or different and are as defined above,

where E_1 and E_2 are taken together with the atoms to which they are attached to form a ring of 5 thru 7 members, optionally containing 3 thru 5

–O-,

-S-,

–N=,

-NX_{1-1}- where X_{1-1} is as defined above,

-CE_2= where E_2 is as defined above,

-C(R_b)$_2$- where R_b is as defined above, and optionally containing 1 or 2 additional double bonds;

-C≡C-E_2 (-C)

where E_2 is as defined above;

-CH_2-CH=CH_2 (-D1)

-CH=C=CH_2 (-D2)

-CH_2-C≡C-H (-D3)

and where R_3, R_4, R_5, R_6, R_9, R_{11} and R_{17} are as defined above, with an agent selected from the group consisting of:

(a) a halogenating agent in the presence of water and a base whose conjugate acid has a pK_a of > about 8,

(b) an oxygen donating agent,

(c) electrochemical oxidation,

(d) a quinone in the presence of water or

(e) nonquinone oxidants; and

(2) contacting the reaction mixture of step (1) with ozone in the presence of an alcohol of the formula R_{7-2}-OH where R_{7-2} is –H and C_1-C_4 alkyl optionally substituted with one or two –OH;

(3) contacting the reaction mixture of step (2) with a hydroperoxy deoxygenating agent and

(4) contacting the reaction mixture of step (3) with an oxidatively cleaving agent.

399. A process to prepare a carboxylic acid (VI) according to claim 398 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is -H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

400. A process to prepare a carboxylic acid (VI) according to claim 399 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

401. A process to prepare a carboxylic acid (VI) according to claim 398 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

402. A process to prepare a carboxylic acid (VI) according to claim 401 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

403. A process to prepare a carboxylic acid (VI) according to claim 398 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

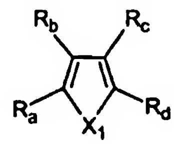
(d) –C≡C-CH_2-O-R_{17-1-1}.

404. A process to prepare a carboxylic acid (VI) according to claim 403 where

R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

405. A process to prepare a carboxylic acid (VI) according to claim 403 where the adduct is of formula (A1)



(A1)

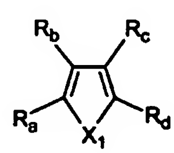
406. A process to prepare a carboxylic acid (VI) according to claim 405 where X_1 is –O-.

407. A process to prepare a carboxylic acid (VI) according to claim 405 where R_b and R_c are –H.

408. A process to prepare a carboxylic acid (VI) according to claim 405 where R_d is C_1 alkyl.

409. A process to prepare a carboxylic acid (VI) according to claim 405 where R_a is –H.

410. A process to prepare a carboxylic acid (VI) according to claim 398 where the adduct is of formula (A2)



(A2)

411. A process to prepare a carboxylic acid (VI) according to claim 410 where

X_1 is –O-.

412. A process to prepare a carboxylic acid (VI) according to claim 410 where R_b and R_d are C_1 alkyl.

413. A process to prepare a carboxylic acid (VI) according to claim 410 where R_c is –H.

414. A process to prepare a carboxylic acid (VI) according to claim 410 where R_a is –H.

415. A process to prepare a carboxylic acid (VI) according to claim 398 where the adduct is (B)

$$R_a\text{-}CE_1\text{=}M \qquad (B)$$

416. A process to prepare a carboxylic acid (VI) according to claim 398 where the adduct is (C)

$$R_a\text{-}C{\equiv}C\text{-}E_2 \qquad (C)$$

417. A process to prepare a carboxylic acid (VI) according to claim 398 where the adduct is selected from the group consisting of (D1), (D2) and (D3)

$$R_a\text{-}CH_2\text{-}CH\text{=}CH_2 \qquad (D1)$$

$$R_a\text{-}CH\text{=}C\text{=}CH_2 \qquad (D2)$$

$$R_a\text{-}CH_2\text{-}C{\equiv}C\text{-}H \qquad (D3)$$

418. A process to prepare a carboxylic acid (VI) according to claim 398 where the oxygen donating agent is selected from the group consisting of:

a peracid,

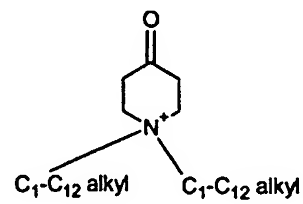
singlet oxygen followed by either phosphite or thiourea,

triplet oxygen,

hydrogen peroxide with a ketone selected from the group consisting of Q_4-CO-Q_5 where Q_4 and Q_5 are the same or different and are

C_1-C_4 alkyl optionally substituted with 1 thru 9 –Cl or –F, and where the

Q_4 and Q_5 are taken together with the attached carbon atom to form a cyclic ketone of 5 thru 7 members and ketones of the formula:



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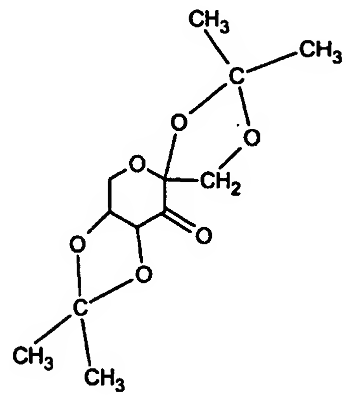


hydrogen peroxide in combination with methyltrioxorhenium,

trichloroacetonitrile/hydrogen peroxide,

trichloroacetamide/hydrogen peroxide,

DDQ/water,

p-chloranil/water,

φ-$C(CH_3)_2$-O-OH or an alkylhydroperoxide in combination with a metal containing activator, where alkyl is from C_4-C_{10} alkyl and metal containing activator is selected from the group consisting of Ti(isopropoxide)$_4$, peroxotungstophosphate, VO(acetylacetonate)$_2$ and MO hexacarbonyl.

419. A process to prepare a carboxylic acid (VI) according to claim 418 where the oxygen donating agent is a peracid.

420. A process to prepare a carboxylic acid (VI) according to claim 419 where the peracid is selected from the group consisting of:

(a) perbenzoic acid optionally substituted with 1 or 2 –Cl or $-NO_2$,

(b) percarboxylic acids of the formula $C_{n2}(Q_6)2_{n2+1}$-CO_3H where n_2 is 1 thru 4 and Q_6 is –H, -Cl or –F,

(c) perphthalic acid and

(d) magnesium peroxyphthalate.

421. A process to prepare a carboxylic acid (VI) according to claim 398 where the halogenating agent is selected from the group consisting of:

dibromodimethylhydantoin,
dichlorodimethylhydantoin,
diiododimethylhydantoin,
N-chlorosuccinamide,
N-bromosuccinamide,
N-iodosuccinamide,
trichloroisocyanuric acid,
t-butylhypochlorite,
3-bromo-1-chloro-5,5-dimethylhydantoin.

422. A process to prepare a carboxylic acid (VI) according to claim 421 where the halogenating agent is dibromodimethylhydantoin.

423. A process to prepare a carboxylic acid (VI) according to claim 398 where at least one equivalent of the halogenating agent is used.

424. A process to prepare a carboxylic acid (VI) according to claim 423 where from about 1.0 to about 1.05 equivalents of the halogenating agent are used.

425. A process to prepare a carboxylic acid (VI) according to claim 398 where the base is selected from the group consisting of acetate, bicarbonate, carbonate, propionate, benzoate, dibasic phosphate and borate.

426. A process to prepare a carboxylic acid (VI) according to claim 425 where the base is acetate.

427. A process to prepare a carboxylic acid (VI) according to claim 398 where the quinone is selected from the group consisting of DDQ, *p*-chloranil and *o*-chloranil.

428. A process to prepare a carboxylic acid (VI) according to claim 427 where the quinone is *p*-chloranil.

429. A process to prepare a carboxylic acid (VI) according to claim 398 where the nonquinone oxidant is selected from the group consisting of Mn^{+3}, Mn^{+7}, Pb^{+4}, Pd^{+2}, Ru^{+8}, Cr^{+6}, ceric ammonium nitrate, iodosobenzene, iodobenzenebistrifluoroacetate, iodobenzenediacetate, tritylfluoroborate.

430. A process to prepare a carboxylic acid (VI) according to claim 398 where the temperature of the reaction mixture for step (2) is from about –100° to about 40°.

431. A process to prepare a carboxylic acid (VI) according to claim 430 where the temperature of the reaction mixture for step (2) is cooled to about –78° to about –20°.

432. A process to prepare a carboxylic acid (VI) according to claim 431 where the temperature of the reaction mixture is cooled to about –50°.

433. A process to prepare a carboxylic acid (VI) according to claim 398 where the cooling is maintained during step (2).

434. A process to prepare a carboxylic acid (VI) according to claim 398 where the ozone is used as an ozone/oxygen mixture.

435. A process to prepare a carboxylic acid (VI) according to claim 398 where the contacting of step (2) is performed by contacting the mixture of step (1), first with the alcohol R_{7-2}-OH, and then with the ozone.

436. A process to prepare a carboxylic acid (VI) according to claim 398 where R_{7-2} is –H, C_1 and iso-C_3.

437. A process to prepare a carboxylic acid (VI) according to claim 436 where R_{7-2} is a mixture of –H, C_1 and iso-C_3.

438. A process to prepare a carboxylic acid (VI) according to claim 398 where the hydroperoxy-deoxygenating agent is selected from the group consisting of:

Q_1Q_2S where Q_1 and Q_2 are the same or different and are

C_1-C_4 alkyl,

phenyl,

bisulfite,

sulfite,

thiosulfate,

tetrahydrothiophene,

(C_1-C_4 alkyl)$_3$ phosphite,

(C_1-C_4 alkyl)$_3$ phosphine,

triphenylphosphine,

hydrosulfite,

thiourea,

butyl vinyl ether,

tetramethylethylene.

zinc and acetic acid,

tetramethylethylene and

2-methylfuran.

439. A process to prepare a carboxylic acid (VI) according to claim 438 where Q_1 and Q_2 are both C_1 alkyl and the hydroperoxy-deoxygenating agent is dimethylsulfide.

440. A process to prepare a carboxylic acid (VI) according to claim 398 where the oxidatively cleaving agent is selected from the group consisting of:

(1) hydrogen peroxide with a carboxylic acid forming agent selected from the group consisting of:

(a) heat,

(b) a base whose conjugate acid has a pK_a of about 5 or above,

(c) an acid which has a pK_a of less than about 3,

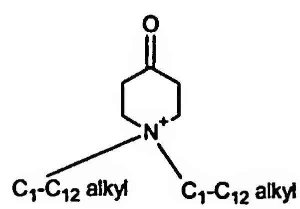
(d) an acylating agent and an acylation catalyst;

(2) $KHSO_5$;

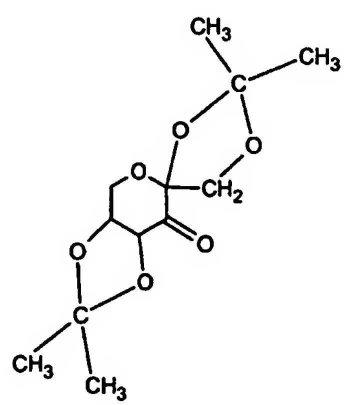
(3) hydrogen peroxide with a ketone selected from the group consisting of Q_4-CO-Q_5 where Q_4 and Q_5 are the same or different and are:

C_1-C_4 alkyl optionally substituted with 1 thru 9 –Cl or –F,

where the Q_4 and Q_5 are taken together with the attached carbon atom to form a cyclic ketone of 5 thru 7 members, and ketones of the formula:



and



(4) hydrogen peroxide in combination with methyltrioxorhenium,

(5) φ-$C(CH_3)_2$-O-OH or an alkylhydroperoxide in combination with a metal containing activator, where alkyl is from C_4-C_{10} alkyl and metal containing activator is selected from the group consisting of Ti(isopropoxide)$_4$, peroxotungstophosphate, VO(acetylacetonate)$_2$ and Mo hexacarbonyl;

(6) peracids selected from the group consisting of

(a) perbenzoic acid optionally substituted with 1 or 2 –Cl or –NO_2,

(b) percarboxylic acids of the formula $C_{n2}(Q_6)2_{n2+1}$-CO_3H where n_2 is 1 thru 4 and Q_6 is –H, -Cl or –F,

(c) perphthalic acid,

(d) magnesium peroxyphthalate.

441. A process to prepare a carboxylic acid (VI) according to claim 440 where the oxidatively cleaving agent is:

(1) hydrogen peroxide with a carboxylic acid forming agent.

442. A process to prepare a carboxylic acid (VI) according to claim 441 where the carboxylic acid forming agent is a base.

443. A process to prepare a carboxylic acid (VI) according to claim 442 where the is base is an inorganic base selected from the group consisting of hydroxide, bicarbonate, and carbonate and organic bases selected from the group consisting of $(Q_3)_3N$ were Q_3 is C_1-C_3 alkyl, DBU, DBN, DABCO, pyridine and *p*-dimethylaminopyridine.

444. A process to prepare a carboxylic acid (VI) according to claim 443 where the base is bicarbonate.

445. A process to prepare a carboxylic acid (VI) according to claim 441 where the carboxylic acid forming agent is an acid.

446. A process to prepare a carboxylic acid (VI) according to claim 445 where the acid is selected from the group consisting of hydrochloric acid, sulfuric acid, phosphoric acid, nitric acid and organic acids of the formula of R_{acid-1}-COOH where R_{acid-1} is –H and C_1-C_3 alkyl optionally substituted with 1 thru 3 –Cl and -F.

447. A process to prepare a carboxylic acid (VI) according to claim 446 where the acid is formic acid and trifluoroacetic acid.

448. A process to prepare a carboxylic acid (VI) according to claim 441 where the carboxylic acid forming agent is an acylating agent.

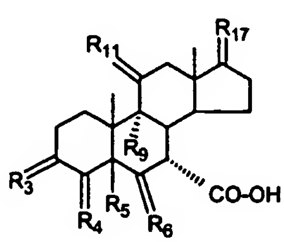
449. A process to prepare a carboxylic acid (VI) according to claim 448 where the acylating agent is the acylating agent is selected from the group consisting of R_{acid-2}-CO-O-CO-R_{acid-2} where R_{acid-2} is –H, C_1-C_3 alkyl optionally substituted with 1 thru 3 –Cl and -F and -φ.

450. A process to prepare a carboxylic acid (VI) according to claim 449 where the acylating agent is acetic anhydride or trifluoracetic anhydride.

451. A process to prepare a carboxylic acid (VI) according to claim 398 where the carboxylic acid (VI) is

17β-hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone.

452. A process to prepare a carboxylic acid of formula (VI)



(VI)

or salt thereof where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

-Si(-CH_3)$_3$,

-Si(-CH_2-CH_3)$_3$,

-CO-CH_3,

-CO-H and

-SiH(CH_3)$_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –Si(R_{17-1-2})$_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) $-C \equiv C-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) $-CH_2-CH_2-CH_2-OH$,

(g) $-CH_2-CH_2-CH_2-O-$(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) $-CH_2-CH_2-CO-O^-$ and where R_{17-2} is $-OH$;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is $-OH$ and where R_{17-4} is:

(a) $-CO-CH_3$,

(b) $-CO-CH_2-OH$,

(c) $-CO-CH_2-O-CO-(CH_2)_{0-3}-CH_3$;

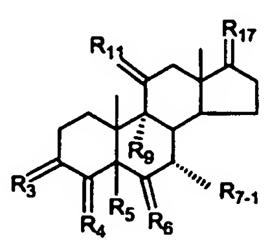
(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing $-O-CH_2-$ where the attachment of the $-O$ is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the $-O$ is at R_{17-8} in the β-orientation;

(6) $-O-CH(OR_{17-9})-CH_2-CH_2$······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is $-H$ or C_1-C_3 alkyl;

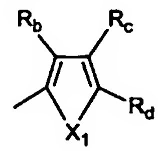
(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}-CH=CH_2$ and R_{17-12} is $-OH$ which comprises:

(1) contacting a 7α-substituted steroid of formula (II)



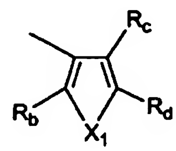
(II)

where R_{7-1} is a molecular fragment of the formula (-A1)



(-A1)

or of the formula (-A2)



(-A2)

where X_1 is:

–S-,

-O- or

–NX_{1-1}- and where X_{1-1} is:

-H,

C_1-C_4 alkyl,

-CO-OX_{1-2} where X_{1-2} is C_1-C_4 alkyl or –CH_2-φ,

-CO-X_{1-2} where X_{1-2} is as defined above,

-CO-φ where –φ is substituted in the *o*-position with –CO-O-(C_1-C_4 alkyl),

-SO_2-(C_1-C_3 alkyl),

-SO_2-φ where φ is optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

–CO-OCH$_3$ and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl;

C_1-C_4 alkoxy;

-CH$_2$-OR_{d-1} where R_{d-1} is –H or C_1-C_4 alkyl,

-CH$_2$-N(R_{d-6})$_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R_{d-6a} where R_{d-6a} is C_1-C_4 alkyl or –φ,

-CH$_2$-O-CO-R_{d-1} where R_{d-1} is as defined above,

-CH(OR_{d-1})$_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

-CH$_2$-CH$_2$-,

-CH$_2$-CH$_2$-CH$_2$-,

-CH$_2$-C(CH$_3$-)$_2$-CH$_2$-,

-CH(-O-CO-R_{d-1})$_2$ where R_{d-1} is as defined above,

-Si(R)$_3$ where R is as defined above,

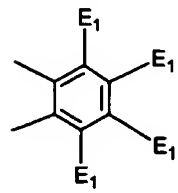
-O-Si(R)$_3$ where R is as defined above,

-Sn(R_{b-1})$_3$ where R_{b-1} is as defined above,

-S-R_{d-5} where R_{d-5} is C_1-C_4 alkyl or –φ,

-N(R_{d-6})$_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

-OE_{1-1} where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

–$SiE_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

-S-E_{1-5} where E_{1-5} is C_1-C_4 alkyl or –φ,

-S-$(O)_{1-2}$-E_{1-5} where E_{1-5} is as defined above,

-$N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are as defined above,

-P(O)(O-E_{1-1})$_2$ where E_{1-1} is as defined above,

-$Si(R)_3$ where R is as defined above;

-CE_1=M (-B)

where E_1 is as defined above and

where M is:

(1) =O,

(2) =N-E_2 where E_2 is selected from the group consisting of

-H

C_1-C_4 alkyl,

C_1-C_4 alkenyl containing 1 or 2 double bonds,

C_1-C_4 alkynyl containing 1 triple bond,

-CO-OE_{2-1} where E_{2-1} is –H or C_1-C_4 alkyl,

$-C(E_{2-1})_2-OE_{2-2}$ where E_{2-1} are the same or different and are as defined above and where E_{2-2} is

C_1-C_4 alkyl,

$-\varphi$ or

$-Si(R)_3$ where the three R are the same or different and are defined above,

$-OE_{2-2}$ where E_{2-2} is as defined above,

$-S-E_{2-3}$ where E_{2-3} is C_1-C_4 alkyl or $-\varphi$,

$-S-(O)_{1-2}-E_{2-3}$ where E_{2-3} is as defined above,

$-N(R_{d-6})_2$ where the two R_{d6} are the same or different and are as defined above;

$-Si(R)_3$ where the three R are as defined above;

(3) $=C(E_2)_2$ where the E_2 are the same or different and are as defined above,

where E_1 and E_2 are taken together with the atoms to which they are attached to form a ring of 5 thru 7 members, optionally containing 3 thru 5

$-O-$,

$-S-$,

$-N=$,

$-NX_{1-1}-$ where X_{1-1} is as defined above,

$-CE_2=$ where E_2 is as defined above,

$-C(R_b)_2-$ where R_b is as defined above, and optionally containing 1 or 2 additional double bonds;

$$-C\equiv C-E_2 \qquad (-C)$$

where E_2 is as defined above;

$$-CH_2-CH=CH_2 \qquad (-D1)$$

$$-CH=C=CH_2 \qquad (-D2)$$

$$-CH_2-C\equiv C-H \qquad (-D3)$$

and where R_3, R_4, R_5, R_6, R_9, R_{11} and R_{17} are as defined above, with

(1) ozone in the presence of an alcohol of the formula $R_{7-2}-OH$ where R_{7-2} is $-H$ and C_1-C_4 alkyl optionally substituted with one or two $-OH$;

(2) contacting the reaction mixture of step (1) with a hydroperoxy deoxygenating agent and

(3) contacting the reaction mixture of step (2) with an oxidatively cleaving agent.

453. A process to prepare a carboxylic acid (VI) according to claim 452 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

454. A process to prepare a carboxylic acid (VI) according to claim 453 where R_3, R_4, R_5 and R_6 are:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H.

455. A process to prepare a carboxylic acid (VI) according to claim 452 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

456. A process to prepare a carboxylic acid (VI) according to claim 455 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and other of R_{11-5} or R_{11-6} is –H.

457. A process to prepare a carboxylic acid (VI) according to claim 452 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

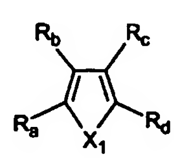
(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

458. A process to prepare a carboxylic acid (VI) according to claim 457 where R_{17} is:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

459. A process to prepare a carboxylic acid (VI) according to claim 452 where the adduct is of formula (A1)



(A1)

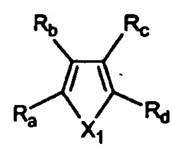
460. A process to prepare a carboxylic acid (VI) according to claim 459 where X_1 is –O-.

461. A process to prepare a carboxylic acid (VI) according to claim 459 where R_b and R_c are –H.

462. A process to prepare a carboxylic acid (VI) according to claim 459 where R_d is C_1 alkyl.

463. A process to prepare a carboxylic acid (VI) according to claim 459 where R_a is –H.

464. A process to prepare a carboxylic acid (VI) according to claim 452 where the adduct is of formula (A2)



(A2)

465. A process to prepare a carboxylic acid (VI) according to claim 464 where X_1 is –O-.

466. A process to prepare a carboxylic acid (VI) according to claim 464 where R_b and R_d are C_1 alkyl.

467. A process to prepare a carboxylic acid (VI) according to claim 464 where R_c is –H.

468. A process to prepare a carboxylic acid (VI) according to claim 464 where R_a is –H.

469. A process to prepare a carboxylic acid (VI) according to claim 452 where

the adduct is (B)

$$R_a\text{-}CE_1\text{=}M \qquad (B)$$

470. A process to prepare a carboxylic acid (VI) according to claim 452 where the adduct is (C)

$$R_a\text{-}C\equiv C\text{-}E_2 \qquad (C)$$

471. A process to prepare a carboxylic acid (VI) according to claim 452 where the adduct is selected from the group consisting of (D1), (D2) and (D3)

$$R_a\text{-}CH_2\text{-}CH\text{=}CH_2 \qquad (D1)$$

$$R_a\text{-}CH\text{=}C\text{=}CH_2 \qquad (D2)$$

$$R_a\text{-}CH_2\text{-}C\equiv C\text{-}H \qquad (D3)$$

472. A process to prepare a carboxylic acid (VI) according to claim 452 where the temperature of the reaction mixture for step (1) is from about –100° to about 40°.

473. A process to prepare a carboxylic acid (VI) according to claim 472 where the temperature of the reaction mixture for step (1) is cooled to about –78° to about –20°.

474. A process to prepare a carboxylic acid (VI) according to claim 473 where the temperature of the reaction mixture is cooled to about –50°.

475. A process to prepare a carboxylic acid (VI) according to claim 472 where the cooling is maintained during step (1).

476. A process to prepare a carboxylic acid (VI) according to claim 452 where the ozone is used as an ozone/oxygen mixture.

477. A process to prepare a carboxylic acid (VI) according to claim 452 where the contacting of step (1) is performed by reacting the 7α-substituted steroid (II) first with the alcohol $R_{7\text{-}2}$-OH, and then with the ozone.

478. A process to prepare a carboxylic acid (VI) according to claim 452 where R_{7-2} is –H, C_1 and iso-C_3.

479. A process to prepare a carboxylic acid (VI) according to claim 478 where R_{7-2} is a mixture of –H, C_1 and iso-C_3.

480. A process to prepare a carboxylic acid (VI) according to claim 452 where the hydroperoxy-deoxygenating agent is selected from the group consisting of:

Q_1Q_2S where Q_1 and Q_2 are the same or different and are

C_1-C_4 alkyl,

phenyl,

bisulfite,

sulfite,

thiosulfate,

tetrahydrothiophene,

(C_1-C_4 alkyl)$_3$ phosphite,

(C_1-C_4 alkyl)$_3$ phosphine,

triphenylphosphine,

hydrosulfite,

thiourea,

butyl vinyl ether,

tetramethylethylene.

zinc and acetic acid,

tetramethylethylene and

2-methylfuran.

481. A process to prepare a carboxylic acid (VI) according to claim 480 where Q_1 and Q_2 are both C_1 alkyl and the hydroperoxy-deoxygenating agent is dimethylsulfide.

482. A process to prepare a carboxylic acid (VI) according to claim 452 where the oxidatively cleaving agent is selected from the group consisting of:

(1) hydrogen peroxide with a carboxylic acid forming agent selected from the group consisting of:

(a) heat,

(b) a base whose conjugate acid has a pK_a of about 5 or above,

(c) an acid which has a pK_a of less than about 3,

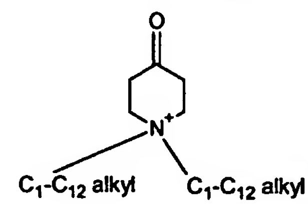
(d) an acylating agent and an acylation catalyst;

(2) $KHSO_5$;

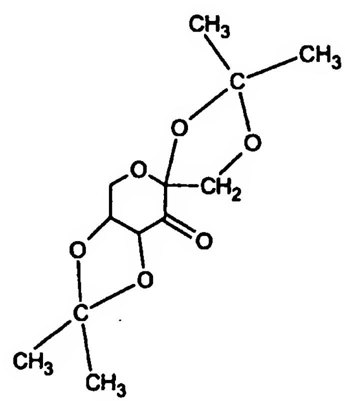
(3) hydrogen peroxide with a ketone selected from the group consisting of Q_4-CO-Q_5 where Q_4 and Q_5 are the same or different and are:

C_1-C_4 alkyl optionally substituted with 1 thru 9 –Cl or –F,

where the Q_4 and Q_5 are taken together with the attached carbon atom to form a cyclic ketone of 5 thru 7 members, and ketones of the formula:



and



(4) hydrogen peroxide in combination with methyltrioxorhenium,

(5) φ-$C(CH_3)_2$-O-OH or an alkylhydroperoxide in combination with a metal containing activator, where alkyl is from C_4-C_{10} alkyl and metal containing activator is selected from the group consisting of Ti(isopropoxide)$_4$, peroxotungstophosphate, VO(acetylacetonate)$_2$ and Mo hexacarbonyl;

(6) peracids selected from the group consisting of

(a) perbenzoic acid optionally substituted with 1 or 2 –Cl or –NO_2,

(b) percarboxylic acids of the formula $C_{n2}(Q_6)2_{n2+1}$-CO_3H where n_2 is 1 thru 4 and Q_6 is –H, -Cl or –F,

(c) perphthalic acid,

(d) magnesium peroxyphthalate.

483. A process to prepare a carboxylic acid (VI) according to claim 482 where the oxidatively cleaving agent is:

(1) hydrogen peroxide with a carboxylic acid forming agent.

484. A process to prepare a carboxylic acid (VI) according to claim 483 where the carboxylic acid forming agent is a base.

485. A process to prepare a carboxylic acid (VI) according to claim 484 where the is base is an inorganic base selected from the group consisting of hydroxide, bicarbonate, and carbonate and organic bases selected from the group consisting of $(Q_3)_3N$ were Q_3 is C_1-C_3 alkyl, DBU, DBN, DABCO, pyridine and *p*-dimethylaminopyridine.

486. A process to prepare a carboxylic acid (VI) according to claim 485 where the base is bicarbonate.

487. A process to prepare a carboxylic acid (VI) according to claim 483 where the carboxylic acid forming agent is an acid.

488. A process to prepare a carboxylic acid (VI) according to claim 487 where the acid is selected from the group consisting of hydrochloric acid, sulfuric acid, phosphoric acid, nitric acid and organic acids of the formula of R_{acid-1}-COOH where R_{acid-1} is –H and C_1-C_3 alkyl optionally substituted with 1 thru 3 –Cl and -F.

489. A process to prepare a carboxylic acid (VI) according to claim 488 where the acid is formic acid and trifluoroacetic acid.

490. A process to prepare a carboxylic acid (VI) according to claim 483 where the carboxylic acid forming agent is an acylating agent.

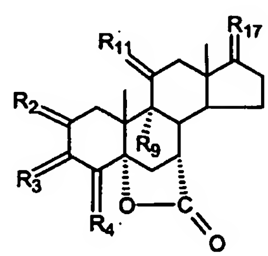
491. A process to prepare a carboxylic acid (VI) according to claim 490 where the acylating agent is the acylating agent is selected from the group consisting of R_{acid-2}-CO-O-CO-R_{acid-2} where R_{acid-2} is –H, C_1-C_3 alkyl optionally substituted with 1 thru 3 –Cl and -F and -φ.

492. A process to prepare a carboxylic acid (VI) according to claim 490 where the acylating agent is acetic anhydride or trifluoracetic anhydride.

493. A process to prepare a carboxylic acid (VI) according to claim 452 where the carboxylic acid (VI) is

17β-hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone.

494. A process to prepare a carboxylic acid (VI) according to claim 452 where the carboxylic acid (VI) is subjected to a reaction medium which has a pH of less than about 5 to obtain a bislactone of formula (VII)



(VII)

where R_2, R_3, R_4, R_9, R_{11} and R_{17} are as defined above.

495. A process to prepare a carboxylic acid (VI) according to claim 494 where the reaction medium contains water and has a pH of less than about 5.

496. A process to prepare a carboxylic acid (VI) according to claim 495 where the reaction medium contains either a strong acid of pK_a less than about 2 or a catalytic amount of base.

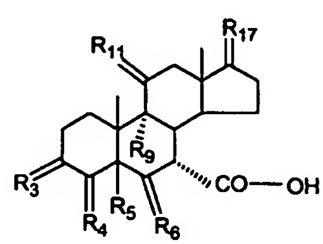
497. A process to prepare a carboxylic acid (VI) according to claim 496 where the carboxylic acid (VI) is reacted with aqueous acid.

498. A process to prepare a carboxylic acid (VI) according to claim 497 where the acid is present in an amount from catalytic to excess.

499. A process to prepare a carboxylic acid (VI) according to claim 497 where the acid is selected from the group consisting of fluorosulfonic, chlorosulfonic, benzenesulfonic, *p*-toluenesulfonic, methanesulfonic, trifluoromethanesulfonic, trifluoroacetic, trichloroacetic, hydrochloric, sulfuric, phosphoric and nitric.

500. A process to prepare a carboxylic acid (VI) according to claim 499 where the benzenesulfonic, *p*-toluenesulfonic or methanesulfonic.

501. A process for the preparation of a carboxylic acid of formula (VI)



(VI)

/

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_9 is:

(1) –H,

(2) –OH,

(3) –O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is selected from the group consisting of:

-Si(-CH_3)$_3$,

-Si(-CH_2-CH_3)$_3$,

-CO-CH_3,

-CO-H and

-SiH(CH_3)$_2$,

(4) –F;

where R_{11} is:

(1) =O,

(2) –H:-H,

(3) α-R_{11-1}:β-R_{11-2} where R_{11-1} is:

(a) –H,

(b) –O-R_{11-3} where R_{11-3} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

and where R_{11-2} is:

(a) –H,

(b) –O-R_{11-4} where R_{11-4} is:

(i) –H,

(ii) a HYDROXY PROTECTING GROUP where HYDROXY PROTECTING GROUP is as defined above,

with the proviso that one of R_{11-1} and R_{11-2} must be –H,

(4) R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H,

(5) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H;

where R_{17} is:

(1) =O;

(2) α-R_{17-1}:β-R_{17-2} where R_{17-1} is:

(a) –H,

(b) –C≡C-H,

(c) –C≡N,

(d) –C≡C-CH_2-O-R_{17-1-1} where R_{17-1-1} is selected from the group consisting of

(i) –H,

(ii) –$Si(R_{17-1-2})_3$ where R_{17-1-2} are the same or different and are C_1-C_4 alkyl,

(iii) 1-ethoxyethyl,

(iv) 2-tetrahydropyranyl,

(e) –C≡C-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(f) –CH_2-CH_2-CH_2-OH,

(g) –CH_2-CH_2-CH_2-O-(HYDROXY PROTECTING GROUP) where HYDROXY PROTECTING GROUP is as defined above,

(h) –CH_2-CH_2-CO-O^- and where R_{17-2} is –OH;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) $-CO-CH_3$,

(b) $-CO-CH_2-OH$,

(c) $-CO-CH_2-O-CO-(CH_2)_{0-3}-CH_3$;

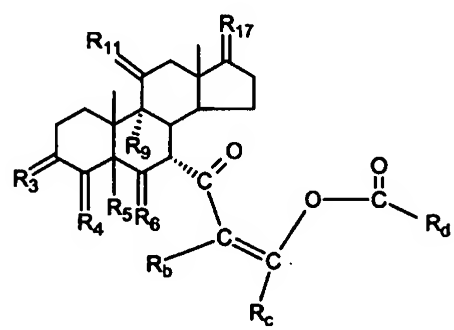
(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing $-O-CH_2-$ where the attachment of the $-O$ is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the $-O$ is at R_{17-8} in the β-orientation;

(6) $-O-CH(OR_{17-9})-CH_2-CH_2\cdots\cdots$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group ($CH_2\cdots\cdots$) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is $-H$ or C_1-C_3 alkyl;

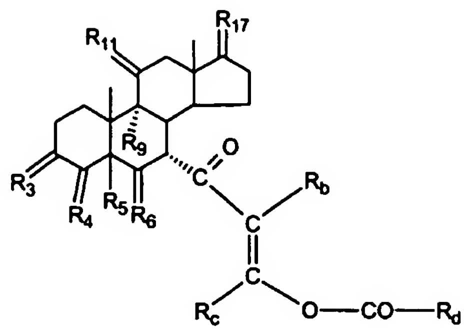
(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}-CH=CH_2$ and R_{17-12} is $-OH$; which comprises:

(1) contacting a cis oxyenedione of the formula (X-*cis*)



(X-cis)

or a trans oxyenedione of the formula (X-*trans*)



(X-trans)

or mixture thereof

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

where R_c is where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

-CO-OCH$_3$ and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl,

C_1-C_4 alkoxy;

-CH$_2$-OR_{d-1} where R_{d-1} is –H or C_1-C_4 alkyl,

-CH$_2$-N(R_{d-6})$_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R_{d-6a} where R_{d-6a} is C_1-C_4 alkyl or –φ,

-CH_2-O-CO-R_{d-1} where R_{d-1} is as defined above,

-CH(OR_{d-1})$_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

-CH_2-CH_2-,

-CH_2-CH_2-CH_2-,

-CH_2-C(CH_3-)$_2$-CH_2-,

-CH(-O-CO-R_{d-1})$_2$ where R_{d-1} is as defined above,

-Si(R)$_3$ where R is as defined above,

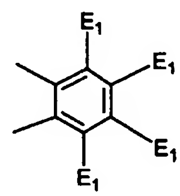
-O-Si(R)$_3$ where R is as defined above,

-Sn(R_{b-1})$_3$ where R_{b-1} is as defined above,

-S-R_{d-5} where R_{d-5} is C_1-C_4 alkyl or –φ,

-N(R_{d-6})$_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

-OE_{1-1} where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

–Si$E_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

-S-E_{1-5} where E_{1-5} is C_1-C_4 alkyl or –φ,

-S-(O)$_{1-2}$-E_{1-5} where E_{1-5} is as defined above,

-$N(R_{4-6})_2$ where the two R_{4-6} are the same or different and are as defined above,

-$P(O)(O-E_{1-1})_2$ where E_{1-1} is as defined above,

-$Si(R)_3$ where R is as defined above,

and where R_3, R_4, R_5, R_6, R_9, R_{11}, R_{17}, are as defined above, with an oxidatively cleaving agent.

502. A process for the preparation of a carboxylic acid (VI) according to claim 501 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-$(CR_{33}R_{34})_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-$(CR_{33}R_{34})_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

503. A process for the preparation of a carboxylic acid (VI) according to claim 501 where R_9 and R_{11} are:

(a) R_{11} is R_{11-5}:R_{11-6} where one of R_{11-5} or R_{11-6} and R_9 are taken together with R_9 to form a second bond between C-9 and C-11 and the other of R_{11-5} or R_{11-6} is –H;

(b) α-R_{11-7}:β-R_{11-8} where R_{11-7} and R_9 are taken together with –O- to form an epoxide between C-9 and C-11 and R_{11-8} is –H,

(c) R_9 is –H and R_{11} is α-R_{11-1}:β-R_{11-2} where R_{11-1} is –O-R_{11-3} where R_{11-3} is –H, and where R_{11-2} is –H.

504. A process for the preparation of a carboxylic acid (VI) according to claim 501 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) α-R_{17-1}:β-R_{17-2} where R_{17-1} is –C≡C-H and where R_{17-2} is –OH;

(d) –C≡C-CH_2-O-R_{17-1-1}.

505. A process for the preparation of a carboxylic acid (VI) according to claim 250 where R_b and R_c are –H.

506. A process for the preparation of a carboxylic acid (VI) according to claim 250 where R_d is C_1 alkyl.

507. A process for the preparation of a carboxylic acid (VI) according to claim 501 where the oxidatively cleaving agent is selected from the group consisting of:

(1) hydrogen peroxide with a carboxylic acid forming agent selected from the group consisting of:

(a) heat,

(b) a base whose conjugate acid has a pK_a of about 5 or above,

(c) an acid which has a pK_a of less than about 3,

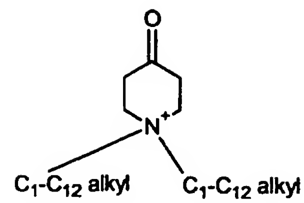
(d) an acylating agent and an acylation catalyst;

(2) $KHSO_5$;

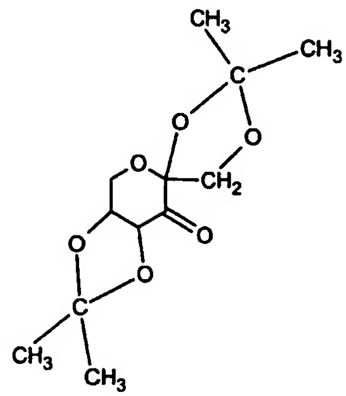
(3) hydrogen peroxide with a ketone selected from the group consisting of Q_4-CO-Q_5 where Q_4 and Q_5 are the same or different and are:

C_1-C_4 alkyl optionally substituted with 1 thru 9 –Cl or –F,

where the Q_4 and Q_5 are taken together with the attached carbon atom to form a cyclic ketone of 5 thru 7 members, and ketones of the formula:



and



(4) hydrogen peroxide in combination with methyltrioxorhenium,

(5) φ-$C(CH_3)_2$-O-OH or an alkylhydroperoxide in combination with a metal containing activator, where alkyl is from C_4-C_{10} alkyl and metal containing activator is selected from the group consisting of Ti(isopropoxide)$_4$, peroxotungstophosphate, VO(acetylacetonate)$_2$ and Mo hexacarbonyl;

(6) peracids selected from the group consisting of

(a) perbenzoic acid optionally substituted with 1 or 2 –Cl or –NO_2,

(b) percarboxylic acids of the formula $C_{n2}(Q_6)2_{n2+1}$-CO_3H where n_2 is 1 thru 4 and Q_6 is –H, -Cl or –F,

(c) perphthalic acid,

(d) magnesium peroxyphthalate.

508. A process for the preparation of a carboxylic acid (VI) according to claim 507 where the oxidatively cleaving agent is:

(1) hydrogen peroxide with a carboxylic acid forming agent.

509. A process for the preparation of a carboxylic acid (VI) according to claim 508 where the carboxylic acid forming agent is a base.

510. A process for the preparation of a carboxylic acid (VI) according to claim 509 where the is base is an inorganic base selected from the group consisting of hydroxide, bicarbonate, and carbonate and organic bases selected from the group consisting of $(Q_3)_3N$ were Q_3 is C_1-C_3 alkyl, DBU, DBN, DABCO, pyridine and *p*-dimethylaminopyridine.

511. A process for the preparation of a carboxylic acid (VI) according to claim 510 where the base is bicarbonate.

512. A process for the preparation of a carboxylic acid (VI) according to claim 508 where the carboxylic acid forming agent is an acid .

513. A process for the preparation of a carboxylic acid (VI) according to claim 512 where the acid is selected from the group consisting of hydrochloric acid, sulfuric acid, phosphoric acid, nitric acid and organic acids of the formula of R_{acid-1}-COOH where R_{acid-1} is –H and C_1-C_3 alkyl optionally substituted with 1 thru 3 –Cl and -F.

514. A process for the preparation of a carboxylic acid (VI) according to claim 513 where the acid is formic acid and trifluoroacetic acid.

515. A process for the preparation of a carboxylic acid (VI) according to claim 508 where the carboxylic acid forming agent is an acylating agent.

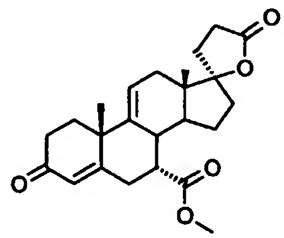
516. A process for the preparation of a carboxylic acid (VI) according to claim 515 where the acylating agent is the acylating agent is selected from the group consisting of R_{acid-2}-CO-O-CO-R_{acid-2} where R_{acid-2} is

–H,

C_1-C_3 alkyl optionally substituted with 1 thru 3 –Cl and -F and -φ.

517. A process for the preparation of a carboxylic acid (VI) according to claim 516 where the acylating agent is acetic anhydride or trifluoracetic anhydride.

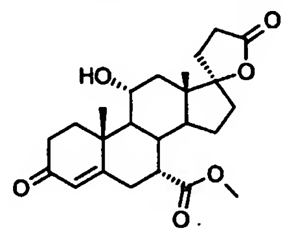
518. A process for the preparation of a $\Delta^{9(11)}$-17-lactone of the formula (CII)



(CII)

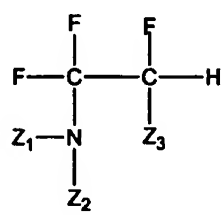
which comprises:

(1) contacting a 11α-hydroxysteroid of formula (CI)



(CI)

with a N-fluoroalkylamine reagent of formula (CVI)



(CVI)

where:

Z_1 is C_1-C_4 alkyl;

Z_2 is C_1-C_4 alkyl and where Z_1 and Z_2 together with the attached nitrogen atom form a 5- or 6-member heterocycle selected from the group consisting of pyrrolidinyl, piperazinyl, piperidinyl and morpholinyl;

Z_3 is –F or –CF_3.

519. A process for the preparation of a $\Delta^{9(11)}$–17-lactone (CII) according to claim 518 where Z_1 and Z_2 are C_1-C_3 alkyl.

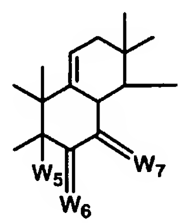
520. A process for the preparation of a $\Delta^{9(11)}$–17-lactone (CII) according to claim 519 where Z_1 and Z_2 are C_1 alkyl.

521. A process for the preparation of a $\Delta^{9(11)}$–17-lactone (CII) according to claim 519 where Z_1 and Z_2 are C_2 alkyl.

522. A process for the preparation of a $\Delta^{9(11)}$–17-lactone (CII) according to claim 521 where the N-fluoroalkylamine (CVI) is N-(1,1,2,3,3,3)hexafluoropropyl)diethylamine.

523. A process for the preparation of a $\Delta^{9(11)}$–17-lactone (CII) according to claim 520 where the N-fluoroalkylamine (CVI) is 1,1,2,2-tetrafluoroethyl-N,N-dimethylamine.

524. A process for the preparation of a $\Delta^{9(11)}$-steroid (CV)



(CV)

where W_5 is:

(1) nothing, there is a double bond between C_4 and C_5;

(2) W_6 is W_{6-1}:W_{6-2} where one of W_{6-1} or W_{6-2} is taken together with W_5 to form a second bond between the carbon atoms to which they are attached and the other of W_{6-1} and W_{6-2} is –H;

(3) W_5 is α-O- and W_7 is α-W_{7-1}:β-W_{7-2} where W_{7-1} is –CO- resulting in a lactone (-O-CO-) with the oxygen atom bonded to the C-5 position in the α-configuration and the carbonyl group bonded to the C-7 position in the α-configuration, W_{7-2} is –H;

where W_6 is:

(1) –H;-H;

(2) is W_{6-3}:W_{6-4} where one of W_{6-3} and W_{6-4} is taken together with W_5 to form a double bond between C-5 and C-6 and the other of W_{6-3} and W_{6-4} is –H;

(3) is W_{6-3}:W_{6-4} and W_7 is W_{7-3}:W_{7-4} where one of W_{6-3} and W_{6-4} is taken together with one of W_{7-3} or W_{7-4} to form a double bond between C-6 and C-7, the other of W_{6-3} and W_{6-4} is –H, the other of W_{7-3} and W_{7-4} is –H;

where W_7 is:

(1) α-W_{7-5}:β-W_{7-6} where W_{7-5} is:

(a) –H,

(b) –C ≡N;

(c) -C ≡C-H,

(d) –CH=CH-CH_3,

(e) –CO-OH,

(f) –CO-OW_{7-5A} where W_{7-5A} is:

(i) C_1-C_4 alkyl,

(ii) –φ optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy,

(g) –φ optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy,

(h) –CO-SW_{7-5A} where W_{7-5A} is as defined above,

(i) -CO-CH=CH-O-CO-W_{7-5A} where W_{7-5A} is as defined above,

(j) –CO-CO-H,

(k) –CH_2-NO_2,

(l) –S-CO-W_{7-5A} where W_{7-5A} is as defined above,

(m) 5-methylfur-2-yl,

(n) 5-*t*-butylfur-2-yl,

and W_{7-6} is –H;

(3) α-W_{7-7}:β-W_{7-8} where W_{7-7} is –H and W_{7-8} is:

(a) –H,

(b) –O-CO-(C_1-C_4 alkyl),

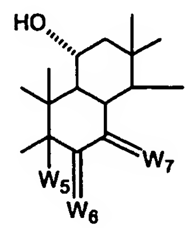
(c) –O-CO-OW_{7-8A} where W_{7-8A} is:

(i) C_1-C_4 alkyl,

(ii) –φ optionally substituted with optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy,

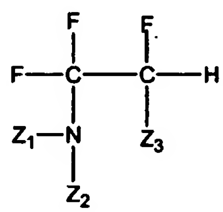
(iii) –CH_2-φ where -φ is optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy; which comprises:

(1) contacting a 11α-hydroxy steroid (CIV)



(CIV)

where W_5, W_6 and W_7 are as defined above, with a N-fluoroalkylamine reagent of the formula (CVI)



(CVI)

where:

Z_1 is C_1-C_4 alkyl;

Z_2 is C_1-C_4 alkyl and where Z_1 and Z_2 together with the attached nitrogen atom form a 5- or 6-member heterocycle selected from the group consisting of pyrrolidinyl, piperazinyl, piperidinyl and morpholinyl;

Z_3 is –F or –CF_3.

525. A process for the preparation of a $\Delta^{9(11)}$-steroid (CV) according to claim 524 where Z_1 and Z_2 are C_1-C_3 alkyl.

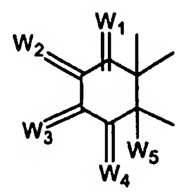
526. A process for the preparation of a $\Delta^{9(11)}$-steroid (CV) according to claim 525 where Z_1 and Z_2 are C_1 alkyl.

527. A process for the preparation of a $\Delta^{9(11)}$-steroid (CV) according to claim 525 where Z_1 and Z_2 are C_2 alkyl.

528. A process for the preparation of a $\Delta^{9(11)}$-steroid (CV) according to claim 527 where the N-fluoroalkylamine (CVI) is N-(1,1,2,3,3,3)hexafluoropropyl)diethylamine.

529. A process for the preparation of a $\Delta^{9(11)}$-steroid (CV) according to claim 526 where the N-fluoroalkylamine (CVI) is 1,1,2,2-tetrafluoroethyl-N,N-dimethylamine.

530. A process for the preparation of a $\Delta^{9(11)}$-steroid (CV) according to claim 524 where the steroid A-ring is



(A-ring)

where:

(1) W_1 is –H:-H and W_2 is –H:-H or W_1 is W_{1-1}:W_{1-2} and W_2 is W_{2-1}:W_{2-2} where one of W_{1-1} or W_{1-2} is taken together with one of W_{2-1} or W_{2-2} to form a second bond between the carbon atoms to which they are attached and the other or W_{1-1} or W_{1-2} and W_{2-1} or W_{2-2} is –H; W_3 is =O, W_4 is W_{4-1}:W_{4-2} where one of W_{4-1} and W_{4-2} is taken together with W_5 to form a second bond between the carbon atoms to which they are attached and the other of W_{4-1} and W_{4-2} is –H;

(2) W_3 is =O, W_4 is –H:-H and W_5 is in the α-orientation and is ·····O-CO- (attached at C_7 to form a 5,7-lactone) and where W_1 and W_2 are as defined above;

(3) W_3 is –O-W_{3-3}:-O-W_{3-4}; W_4 is W_{4-3}:W_{4-4}, where one of W_{4-3} and W_{4-4} is taken together with W_5 to form a second bond between the atoms to which they are attached and the other of W_{4-3} and W_{4-4} is –H; W_{3-3} and W_{3-4} are:

(a) the same or different and are C_1-C_5 alkyl,

(b) taken together to form a cyclic moiety selected from the group consisting of:

(i) $-CH_2-CH_2-$,

(ii) $-CH_2-CH_2-CH_2-$,

(iii) $-CH_2-C(CH_3)_2-CH_2-$; and where W_1 and W_2 are as defined above;

(4) W_3 is $-O-W_{3-3}:-O-W_{3-4}$; W_4 is $-H:-H$; W_5 forms a second bond between C_5 and C_6; W_{3-3} and W_{3-4} are as defined above:

(5) W_3 is $W_{3-5}:W_{3-6}$; where

(a) one of W_{3-5} and W_{3-6} is $-H$ and the other of W_{3-5} and W_{3-6} is:

(i) $-O-W_{3-5A}$ where W_{3-5A} is C_1-C_3 alkyl,

(ii) $-O-CO-W_{3-5A}$ where W_{3-5A} is as defined above,

(iii) $-N(W_{3-5A})_2$ where W_{3-5A} is as defined above,

(iv) piperazinyl,

(v) morpholinyl,

(vi) piperidinyl,

(vii) $-O-CO-O-W_{3-5B}$ where W_{3-5B} is

(aa) C_1-C_4 alkyl,

(bb) $-\varphi$ optionally substituted with optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy,

(cc) $-CH_2-\varphi$ where $-\varphi$ is optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy;

(b) W_{3-5} and W_{3-6} are taken together with the carbon atom to which they are attached to form a cyclic moiety including:

(i) $-O-CH_2-CH_2-O-$,

(ii) $-O-CH_2-CH_2-CH_2-O-$,

(iii) $-O-CH_2-C(CH_3)_2-CH_2-O-$ and where W_4 is $-H:-H$; W_5 forms a second bond between C_5 and C_6;

(6) W_3 is $W_{3-7}:W_{3-8}$ and where W_4 is $W_{4-7}:W_{4-8}$ where

(a) one of W_{3-7} and W_{3-8} is:

(i) $-O-$ W_{3-7A} where W_{3-7A} is C_1-C_3 alkyl,

(ii) $-O-CO-W_{3-7A}$ where W_{3-7A} is as defined above,

(iii) $-N(W_{3-7A})_2$ where W_{3-7A} is as defined above,

(iv) piperazinyl,

(v) morpholinyl,

(vi) piperidinyl, and where the other of W_{3-7} and W_{3-8} is taken together with one of W_{4-7} and W_{4-8} to form a second bond between the carbon

atoms to which they are attached and the other of W_{4-7} and W_{4-8} is –H; W_5 forms a second bond between C_5 and C_6;

(vii) –O-CO-O-W_{3-5B} where W_{3-5B} is as defined above;

(7) W_3 is α-W_{3-9}:β-W_{3-10}; where W_{3-9} is –H and W_{3-10} is:

(a) –O-CO-W_{3-10A} where W_{3-10A} is C_1-C_3 alkyl,

(b) –O-CO-O-W_{3-10B} where W_{3-10B} is

(i) C_1-C_4 alkyl,

(ii) –φ optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy,

(iii) –CH_2-φ where φ is optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy; where WR_4 is –H:-H; and W_5 forms a second bond between the carbon atoms at C_5 and C_6; and where W_1 and W_2 are as defined above;

(8) W_3 is α-W_{3-9}:β-W_{3-10}; where W_4 is W_{4-9}:W_{4-10} where W_{3-9} and W_{3-10} are as defined above; where one of W_{4-9} and W_{4-10} taken together with W_5 forms a second bond between the atoms to which they are attached and the other of W_{4-9} and W_{4-10} is –H; and where W_1 and W_2 are as defined above.

531. A process for the preparation of a $\Delta^{9(11)}$-compound (IV) according to claim 530 where the steroid A-ring is

(1) W_1 is –H:-H and W_2 is –H:-H or W_1 is W_{1-1}:W_{1-2} and W_2 is W_{2-1}:W_{2-2} where one of W_{1-1} or W_{1-2} is taken together with one of W_{2-1} or W_{2-2} to form a second bond between the carbon atoms to which they are attached and the other or W_{1-1} or W_{1-2} and W_{2-1} or W_{2-2} is –H; W_3 is =O, W_4 is W_{4-1}:W_{4-2} where one of W_{4-1} and W_{4-2} is taken together with W_5 to form a second bond between the carbon atoms to which they are attached and the other of W_{4-1} and W_{4-2} is –H;

(2) W_3 is α-W_{3-9}:β-W_{3-10}; where W_{3-9} is –H and W_{3-10} is:

(a) –O-CO-O-W_{3-10A} where W_{3-10A} is C_1-C_3 alkyl,

(b) –CO-O-W_{3-10B} where W_{3-10B} is

(i) C_1-C_4 alkyl,

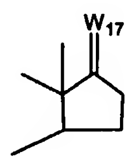
(ii) –φ optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy,

(iii) $-CH_2-\varphi$ where φ is optionally substituted with one thru three C_1-C_3 alkyl, -F, -Cl, -Br, -I, C_1-C_3 alkoxy; where WR_4 is –H:-H; and W_5 forms a second bond between the carbon atoms at C_5 and C_6; and where W_1 and W_2 are as defined above.

532. A process for the preparation of a $\Delta^{9(11)}$-steroid (CV) according to claim 531 where the steroid A-ring is

(1) W_1 is –H:-H and W_2 is –H:-H or W_1 is W_{1-1}:W_{1-2} and W_2 is W_{2-1}:W_{2-2} where one of W_{1-1} or W_{1-2} is taken together with one of W_{2-1} or W_{2-2} to form a second bond between the carbon atoms to which they are attached and the other or W_{1-1} or W_{1-2} and W_{2-1} or W_{2-2} is –H; W_3 is =O, W_4 is W_{4-1}:W_{4-2} where one of W_{4-1} and W_{4-2} is taken together with W_5 to form a second bond between the carbon atoms to which they are attached and the other of W_{4-1} and W_{4-2} is –H;

533. A process for the preparation of a $\Delta^{9(11)}$-steroid (CV) according to claim 524 where the steroid D-ring is



(D-ring)

where W_{17} is:

(1) =O,

(2) α-W_{17-1}:β-W_{17-2} where:

(a) W_{17-1} and W_{17-2} are taken together with the attached carbon atom to form an epoxide of the formula ····CH_2-O–,

(b) W_{17-1} and W_{17-2} are taken together with the attached carbon atom to form a lactone of the formula ····CH_2-CH_2-CO-O–;

(3) α-W_{17-3}:β-W_{17-4} where

(a) W_{17-3} is:

(i) –H,

(ii) –O-CO-W_{17-3A} where W_{17-3A} is –H or –CO-W_{17-3B} where W_{17-3B} is C_1-C_4 alkyl or –φ and

(b) W_{17-4} is –CO-CH_3;

(4) α-W_{17-5}:β-W_{17-6} where

(a) W_{17-5} is:

(i) –O-CO-W_{17-5A} where W_{17-5A} is C_1-C_4 alkyl or –φ,

(b) W_{17-6} is:

(i) –CO-CH_2-O-W_{17-6A} where W_{17-6A} is C_1-C_4 alkyl or –φ.

534. A process for the preparation of a $\Delta^{9(11)}$-steroid (CV) according to claim 533 where W_{17} is:

(1) =O,

(2) α-W_{17-1}:β-W_{17-2} where:

(a) W_{17-1} and W_{17-2} are taken together with the attached carbon atom to form an epoxide of the formula ····CH_2-O–,

(b) W_{17-1} and W_{17-2} are taken together with the attached carbon atom to form a lactone of the formula ····CH_2-CH_2-CO-O–.

535. A process for the preparation of a $\Delta^{9(11)}$-steroid (CV) according to claim 534 where W_{17} is:

(1) =O,

(2) α-W_{17-1}:β-W_{17-2} where:

(b) W_{17-1} and W_{17-2} are taken together with the attached carbon atom to form a lactone of the formula ····CH_2-CH_2-CO-O–.

536. A process for the preparation of a $\Delta^{9(11)}$-steroid (CV) according to claim 533 where W_{17} is:

(3) α-W_{17-3}:β-W_{17-4} where

(a) W_{17-3} is:

(i) –H,

(ii) –O-CO-W_{17-3A} where W_{17-3A} is –H or –CO-W_{17-3B} where W_{17-3B} is C_1-C_4 alkyl or –φ and

(b) W_{17-4} is –CO-CH_3.

537. A process for the preparation of a $\Delta^{9(11)}$-compound (IV) according to claim 533 where W_{17} is:

(4) α-W_{17-5}:β-W_{17-6} where

(a) W_{17-5} is:

(i) –O-CO-W_{17-5A} where W_{17-5A} is C_1-C_4 alkyl or –φ,

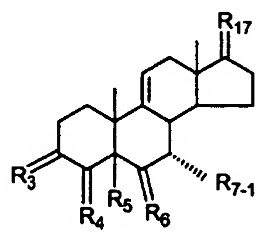
(b) W_{17-6} is:

(i) –CO-CH_2-O-W_{17-6A} where W_{17-6A} is C_1-C_4 alkyl or –φ.

538. A process for the preparation of a $\Delta^{9(11)}$-steroid (CV) according to claim 524 where the $\Delta^{9(11)}$-steroid (CV) is

17β-hydroxypregna-4,9(11)-dien-3-one-7α,21-dicarboxylic acid, γ-lactone, methyl ester.

539. A process for the preparation of a $\Delta^{9(11)}$-7α-substituted steroid of the formula (II)



(II)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(II) R_3 is R_{3-3}:R_{3-4} and R_4 is R_{4-3}:R_{4-4} where one of R_{3-3} and R_{3-4} is –O-R_{31} where R_{31} is C_1-C_3 alkyl, the other of R_{3-3} and R_{3-4} is taken together with one of R_{4-3} and R_{4-4} to form a second bond between the carbon atoms to which they are attached, and the other of R_{4-3} and R_{4-4} is –H; R_6 is R_{6-3}:R_{6-4} where one of R_{6-3} and R_{6-4} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-3} and R_{6-4} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

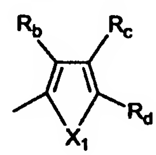
$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

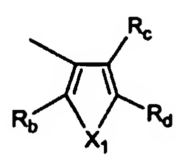
(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_{7-1} is a molecular fragment of the formula (-A1)



(-A1)

or of the formula (-A2)



(-A2)

where X_1 is:

–S-,

-O- or

–NX_{1-1}- and where X_{1-1} is:

-H,

C_1-C_4 alkyl,

-CO-OX_{1-2} where X_{1-2} is C_1-C_4 alkyl or –CH_2-φ,

-CO-X_{1-2} where X_{1-2} is as defined above,

-CO-φ where –φ is substituted in the *o*-position with –CO-O-(C_1-C_4 alkyl),

$-SO_2-(C_1-C_3$ alkyl),

$-SO_2-\varphi$ where φ is optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

$-O-Si(R)_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, $-\varphi$, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

$-CO-OCH_3$ and

$-CO-R_{c-1}$ where R_{c-1} is C_1-C_4 alkyl or $-\varphi$;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl;

C_1-C_4 alkoxy;

$-CH_2-OR_{d-1}$ where R_{d-1} is –H or C_1-C_4 alkyl,

$-CH_2-N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

$-\varphi$,

$-CO-R_{d-6a}$ where R_{d-6a} is C_1-C_4 alkyl or $-\varphi$,

$-CH_2-O-CO-R_{d-1}$ where R_{d-1} is as defined above,

-CH(OR_{d-1})$_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

-CH_2-CH_2-,

-CH_2-CH_2-CH_2-,

-CH_2-C(CH_3-)$_2$-CH_2-,

-CH(-O-CO-R_{d-1})$_2$ where R_{d-1} is as defined above,

-Si(R)$_3$ where R is as defined above,

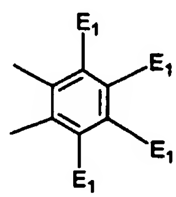
-O-Si(R)$_3$ where R is as defined above,

-Sn(R_{b-1})$_3$ where R_{b-1} is as defined above,

-S-R_{d-5} where R_{d-5} is C_1-C_4 alkyl or –φ,

-N(R_{d-6})$_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

-OE_{1-1} where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

–Si$E_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

-S-E_{1-5} where E_{1-5} is C_1-C_4 alkyl or –φ,

-S-(O)$_{1-2}$-E_{1-5} where E_{1-5} is as defined above,

-N(R_{d-6})$_2$ where the two R_{d-6} are the same or different and are as defined above,

-P(O)(O-E_{1-1})$_2$ where E_{1-1} is as defined above,

-Si(R)$_3$ where R is as defined above;

$-CE_1=M$ (-B)

where E_1 is as defined above and

where M is:

(1) =O,

(2) $=N-E_2$ where E_2 is selected from the group consisting of

-H

C_1-C_4 alkyl,

C_1-C_4 alkenyl containing 1 or 2 double bonds,

C_1-C_4 alkynyl containing 1 triple bond,

$-CO-OE_{2-1}$ where E_{2-1} is –H or C_1-C_4 alkyl,

$-C(E_{2-1})_2-OE_{2-2}$ where E_{2-1} are the same or different and are as defined above and where E_{2-2} is

C_1-C_4 alkyl,

-φ or

$-Si(R)_3$ where the three R are the same or different and are defined above,

$-OE_{2-2}$ where E_{2-2} is as defined above,

$-S-E_{2-3}$ where E_{2-3} is C_1-C_4 alkyl or –φ,

$-S-(O)_{1-2}-E_{2-3}$ where E_{2-3} is as defined above,

$-N(R_{d-6})_2$ where the two R_{d6} are the same or different and are as defined above;

$-Si(R)_3$ where the three R are as defined above;

(3) $=C(E_2)_2$ where the E_2 are the same or different and are as defined above,

where E_1 and E_2 are taken together with the atoms to which they are attached to form a ring of 5 thru 7 members, optionally containing 3 thru 5

–O-,

-S-,

–N=,

$-NX_{1-1}-$ where X_{1-1} is as defined above,

$-CE_2=$ where E_2 is as defined above,

$-C(R_b)_2-$ where R_b is as defined above, and optionally containing 1 or 2 additional double bonds;

$$-C{\equiv}C-E_2 \qquad \text{(-C)}$$

where E_2 is as defined above;

$$-CH_2-CH{=}CH_2 \qquad \text{(-D1)}$$

$$-CH{=}C{=}CH_2 \qquad \text{(-D2)}$$

$$-CH_2-C{\equiv}C-H \qquad \text{(-D3)}$$

where R_{17} is:

(1) =O;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) $-CO-CH_3$,

(b) $-CO-CH_2-OH$,

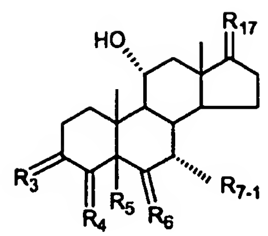
(c) $-CO-CH_2-O-CO-(CH_2)_{0-3}-CH_3$;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing $-O-CH_2-$ where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing $-O-CO-CH_2-CH_2-$ where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

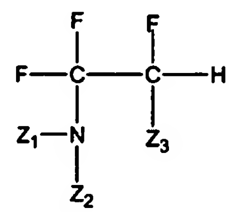
(6) $-O-CH(OR_{17-9})-CH_2-CH_2\cdots\cdots$ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group ($CH_2\cdots\cdots$) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is $-(CH_2)_{1-2}-CH{=}CH_2$ and R_{17-12} is –OH; which comprises contacting a 11α-hydroxy 7α-substituted steroid of the formula (II)



(II)

where R_3, R_4, R_5, R_6 R_{7-1} and R_{17} are as defined above, with a N-fluoroalkylamine reagent of the formula (CVI)



(CVI)

where:

Z_1 is C_1-C_4 alkyl;

Z_2 is C_1-C_4 alkyl and where Z_1 and Z_2 together with the attached nitrogen atom form a 5- or 6-member heterocycle selected from the group consisting of pyrrolidinyl, piperazinyl, piperidinyl and morpholinyl;

Z_3 is –F or –CF_3.

540. A process for the preparation of a $\Delta^{9(11)}$-7α-substituted steroid (II) according to claim 539 where Z_1 and Z_2 are C_1-C_3 alkyl.

541. A process for the preparation of a $\Delta^{9(11)}$-7α-substituted steroid (II) according to claim 540 where Z_1 and Z_2 are C_1 alkyl.

542. A process for the preparation of a $\Delta^{9(11)}$-7α-substituted steroid (II) according to claim 540 where Z_1 and Z_2 are C_2 alkyl.

543. A process for the preparation of a $\Delta^{9(11)}$-7α-substituted steroid (II) according to claim 542 where the N-fluoroalkylamine (CVI) is N-(1,1,2,3,3,3)hexafluoropropyl)diethylamine.

544. A process for the preparation of a $\Delta^{9(11)}$-7α-substituted steroid (II) according to claim 541 where the N-fluoroalkylamine (CVI) is 1,1,2,2-tetrafluoroethyl-N,N-dimethylamine.

545. A process for the preparation of a $\Delta^{9(11)}$-7α-substituted steroid (II) according to claim 539 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

546. A process for the preparation of a $\Delta^{9(11)}$-7α-substituted steroid (II) according to claim 539 where R_{17} is selected from the group consisting of:

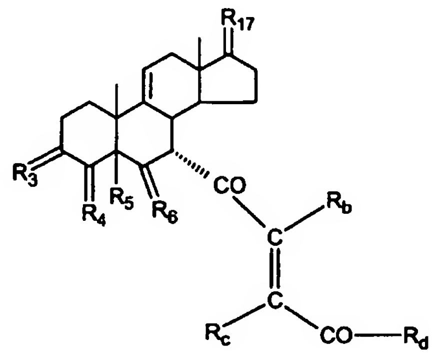
(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) –C≡C-CH_2-O-R_{17-1-1}.

547. A process for the preparation of a $\Delta^{9(11)}$-7α-substituted steroid (II) according to claim 539 where the $\Delta^{9(11)}$-7α-substituted steroid (II) is 17β-hydroxy-7α-(5'-methyl-2'-furyl)-pregna-4,9-dien-3-one-21-carboxylic acid, γ-lactone.

548. A process for the preparation of a $\Delta^{9(11)}$-trans enedione of the formula (III-*trans*)



(III-trans)

where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

$$-(CH_2)-(CR_{33}R_{34})_{n1}-(CH_2)-$$

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_{17} is:

(1) =O;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-$(CH_2)_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-CH_2······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2······) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is –$(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH;

where R_b is selected from the group consisting of

–H,

C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

where R_c is selected from the group consisting of:

-H,

C_1-C_4 alkyl,

C_1-C_4 alkoxy,

-O-Si(R)$_3$ where the R's are the same or different and are –H, C_1-C_4 alkyl, -φ, C_1-C_4 alkoxy and –OH,

-F, -Cl, -Br, -I,

-CO-OCH$_3$ and

-CO-R_{c-1} where R_{c-1} is C_1-C_4 alkyl or –φ;

where R_d is selected from the group consisting of

–H,

-C≡N,

C_1-C_{10} alkyl;

C_1-C_4 alkoxy;

-CH$_2$-OR_{d-1} where R_{d-1} is –H or C_1-C_4 alkyl,

-CH$_2$-N(R_{d-6})$_2$ where the two R_{d-6} are the same or different and are:

C_1-C_4 alkyl,

-φ,

-CO-R_{d-6a} where R_{d-6a} is C_1-C_4 alkyl or –φ,

-CH$_2$-O-CO-R_{d-1} where R_{d-1} is as defined above,

-CH(OR_{d-1})$_2$ where R_{d-1} is as defined above and where the two R_{d-1} taken together are:

-CH$_2$-CH$_2$-,

-CH$_2$-CH$_2$-CH$_2$-,

-CH$_2$-C(CH$_3$-)$_2$-CH$_2$-,

-CH(-O-CO-R_{d-1})$_2$ where R_{d-1} is as defined above,

-Si(R)$_3$ where R is as defined above,

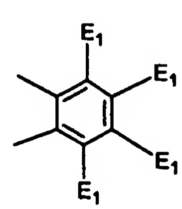
-O-Si(R)$_3$ where R is as defined above,

-Sn(R_{b-1})$_3$ where R_{b-1} is as defined above,

-S-R_{d-5} where R_{d-5} is C_1-C_4 alkyl or –φ,

-N(R_{d-6})$_2$ where R_{d-6} is as defined above,

where R_c and R_d taken together with the atoms to which they are attached to form



where E_1 are the same or different and are:

-H,

C_1-C_4 alkyl,

-F, -Cl, -Br, -I,

-OE_{1-1} where E_{1-1} is:

-H,

C_1-C_4 alkyl,

-φ or

–$SiE_{1-2}E_{1-3}E_{1-4}$ where E_{1-2}, E_{1-3} and E_{1-4} are the same or different and are C_1-C_4 alkyl or C_1-C_4 alkoxy,

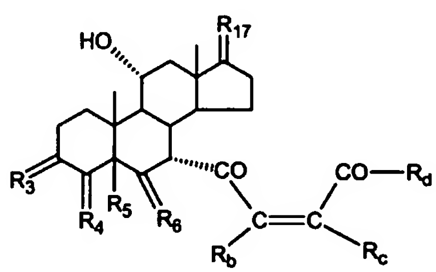
-S-E_{1-5} where E_{1-5} is C_1-C_4 alkyl or –φ,

-S-$(O)_{1-2}$-E_{1-5} where E_{1-5} is as defined above,

-$N(R_{d-6})_2$ where the two R_{d-6} are the same or different and are as defined above,

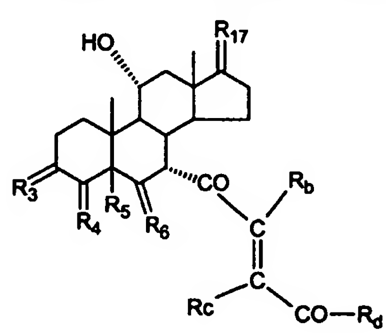
-$P(O)(O\text{-}E_{1-1})_2$ where E_{1-1} is as defined above,

-$Si(R)_3$ where R is as defined above, which comprises contacting a 11α-hydroxy cis enedione of the formula (III-*cis*)



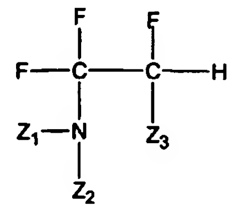
(III-cis)

or a 11α-hydroxy trans enedione of the formula (III-*trans*)



(III-trans)

where R_3, R_4, R_5, R_6, R_{17}, R_b, R_c and R_d are as defined above, with a N-fluoroalkylamine reagent of the formula (CVI)



(CVI)

where:

Z_1 is C_1-C_4 alkyl;

Z_2 is C_1-C_4 alkyl and where Z_1 and Z_2 together with the attached nitrogen atom form a 5- or 6-member heterocycle selected from the group consisting of pyrrolidinyl, piperazinyl, piperidinyl and morpholinyl;

Z_3 is $-F$ or $-CF_3$.

549. A process for the preparation of a $\Delta^{9(11)}$-trans enedione of the formula (III-*trans*) according to claim 548 where Z_1 and Z_2 are C_1-C_3 alkyl.

550. A process for the preparation of a $\Delta^{9(11)}$-trans enedione of the formula (III-*trans*) according to claim 549 where Z_1 and Z_2 are C_1 alkyl.

551. A process for the preparation of a $\Delta^{9(11)}$-trans enedione of the formula (III-*trans*) according to claim 549 where Z_1 and Z_2 are C_2 alkyl.

552. A process for the preparation of a $\Delta^{9(11)}$-trans enedione of the formula (III-*trans*) according to claim 551 where the N-fluoroalkylamine (CVI) is N-(1,1,2,3,3,3)hexafluoropropyl)diethylamine.

553. A process for the preparation of a $\Delta^{9(11)}$-trans enedione of the formula (III-*trans*) according to claim 550 where the N-fluoroalkylamine (CVI) is 1,1,2,2-tetrafluoroethyl-N,N-dimethylamine.

554. A process for the preparation of a $\Delta^{9(11)}$-trans enedione of the formula (III-*trans*) according to claim 548 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is $=O$; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

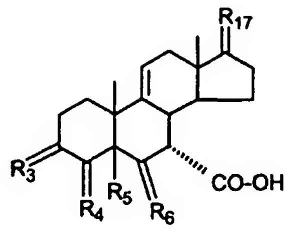
555. A process for the preparation of a $\Delta^{9(11)}$-trans enedione of the formula (III-*trans*) according to claim 548 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(b) =O;

(c) –C≡C-CH_2-O-R_{17-1-1}.

556. A process to prepare a $\Delta^{9(11)}$-carboxylic acid of the formula (VI)



(VI)

or salt thereof where

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is –H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are the same or different and are selected from the group consisting of

C_1-C_3 alkyl and

R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 or 6 atoms of the formula

-(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)-

where n_1 is 0 or 1;

where R_{33} and R_{34} are the same or different and are –H and C_1-C_3 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(IV) R_3 is α-R_{3-7}:β-R_{3-8} where R_{3-7} is –O-R_{31} and R_{3-8} is –O-R_{32} where R_{31} and R_{32} are as defined above; R_4 is R_{4-7}:R_{4-8} where one of R_{4-7} and R_{4-8} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{4-7} and R_{4-8} is –H; R_6 is –H:-H;

where R_{17} is:

(1) =O;

(3) α-R_{17-3}:β-R_{17-4} where R_{17-3} is –OH and where R_{17-4} is:

(a) –CO-CH_3,

(b) –CO-CH_2-OH,

(c) –CO-CH_2-O-CO-(CH_2)$_{0-3}$-CH_3;

(4) α-R_{17-5}:β-R_{17-6} where R_{17-5} and R_{17-6} are taken with the attached carbon atom to form a three member epoxide containing –O-CH_2- where the

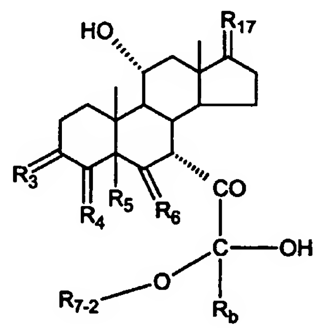
attachment of the –O is at R_{17-6} in the β-orientation and the attachment of the CH_2- is at R_{17-5} in the α-orientation;

(5) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation;

(6) –O-CH(OR_{17-9})-CH_2-CH_2······ where the bond from the oxygen (-O) is one of the four bonds at C-17 in the β-configuration and the bond from the methylene group (CH_2·····) is another of the four bonds at C-17 in the α-configuration to form a 5 member heterocycle containing one oxygen atom, where R_{17-9} is –H or C_1-C_3 alkyl;

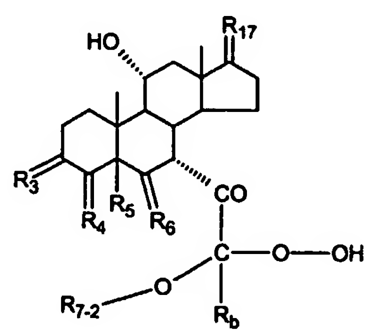
(7) α-R_{17-11}:β-R_{17-12} where R_{17-10} is –$(CH_2)_{1-2}$-CH=CH_2 and R_{17-12} is –OH which comprises

(1) contacting a 11α-hydroxy-hydroxy compound of the formula (IV-OH)



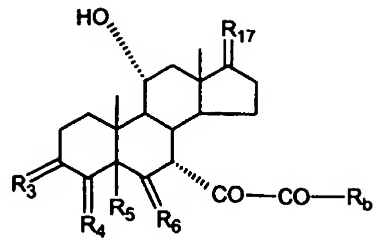
(IV-OH)

or a 11α-hydroxy-hydroperoxy compound of the formula (IV-OOH)



(IV-OOH)

or a 11α-hydroxy biscarbonyl compound of the formula (V)



(V)

where R_b is selected from the group consisting of

–H,

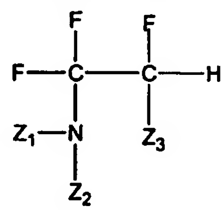
C_1-C_4 alkyl or

phenyl optionally substituted with 1 or 2

C_1-C_4 alkyl,

C_1-C_4 alkoxy;

where R_{7-2} is –H and C_1-C_4 alkyl optionally substituted with one or two –OH, and where R_3, R_4, R_5, R_6 and R_{17} are as defined above, with a N-fluoroalkylamine reagent of the formula (CVI)



(CVI)

where:

Z_1 is C_1-C_4 alkyl;

Z_2 is C_1-C_4 alkyl and where Z_1 and Z_2 together with the attached nitrogen atom form a 5- or 6-member heterocycle selected from the group consisting of pyrrolidinyl, piperazinyl, piperidinyl and morpholinyl;

Z_3 is –F or –CF_3;

(2) contacting the reaction mixture of step (1) with an oxidatively cleaving agent.

557. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 556 where Z_1 and Z_2 are C_1-C_3 alkyl.

558. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 557 where Z_1 and Z_2 are C_1 alkyl.

559. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 557 where Z_1 and Z_2 are C_2 alkyl.

560. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 559 where the N-fluoroalkylamine (CVI) is N-(1,1,2,3,3,3)hexafluoropropyl)diethylamine.

561. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 558 where the N-fluoroalkylamine (CVI) is 1,1,2,2-tetrafluoroethyl-N,N-dimethylamine.

562. process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 556 where R_3, R_4, R_5 and R_6 are selected from the group consisting of:

(I) R_3 is = O; R_4 is R_{4-1}:R_{4-2} where one of R_{4-1} and R_{4-2} is –H and the other of R_{4-1} and R_{4-2} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached; R_6 is -H:-H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 5 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 0; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H;

(III) R_3 is α-R_{3-5}:β-R_{3-6} where R_{3-5} is –O-R_{31} and R_{3-6} is –O-R_{32} where R_{31} and R_{32} are taken with the attached –O-C-O- to form a cyclic ketal of 6 atoms of the formula -(CH_2)-($CR_{33}R_{34}$)$_{n1}$-(CH_2)- where n_1 is 1 and R_{33} and R_{34} are both C_1 alkyl; R_4 is –H:-H; R_6 is R_{6-5}:R_{6-6} where one of R_{6-5} and R_{6-6} is taken together with R_5 to form a second bond between the carbon atoms to which they are attached and the other of R_{6-5} and R_{6-6} is –H.

563. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 556 where R_{17} is selected from the group consisting of:

(a) α-R_{17-7}:β-R_{17-8} where R_{17-7} and R_{17-8} are taken with the attached carbon atom to form a five member lactone containing –O-CO-CH_2-CH_2- where the attachment of the CH_2- is at R_{17-7} in the α-orientation and the attachment of the –O is at R_{17-8} in the β-orientation.

(b) =O;

(c) –C≡C-CH_2-O-R_{17-1-1}.

564. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 556 where the oxidatively cleaving agent is selected from the group consisting of:

(1) hydrogen peroxide with a carboxylic acid forming agent selected from the group consisting of:

(a) heat,

(b) a base whose conjugate acid has a pK_a of about 5 or above,

(c) an acid which has a pK_a of less than about 3,

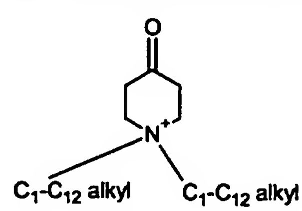
(d) an acylating agent and an acylation catalyst;

(2) $KHSO_5$;

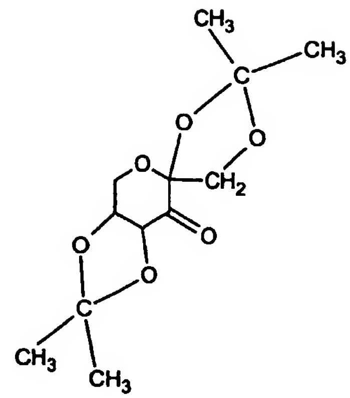
(3) hydrogen peroxide with a ketone selected from the group consisting of Q_4-CO-Q_5 where Q_4 and Q_5 are the same or different and are:

C_1-C_4 alkyl optionally substituted with 1 thru 9 –Cl or –F,

where the Q_4 and Q_5 are taken together with the attached carbon atom to form a cyclic ketone of 5 thru 7 members, and ketones of the formula:



and



(4) hydrogen peroxide in combination with methyltrioxorhenium,

(5) φ-$C(CH_3)_2$-O-OH or an alkylhydroperoxide in combination with a metal containing activator, where alkyl is from C_4-C_{10} alkyl and metal containing activator is selected from the group consisting of Ti(isopropoxide)$_4$, peroxotungstophosphate, VO(acetylacetonate)$_2$ and Mo hexacarbonyl;

(6) peracids selected from the group consisting of

(a) perbenzoic acid optionally substituted with 1 or 2 –Cl or –NO_2,

(b) percarboxylic acids of the formula $C_{n2}(Q_6)2_{n2+1}$-CO_3H where n_2 is 1 thru 4 and Q_6 is –H, -Cl or –F,

(c) perphthalic acid,

(d) magnesium peroxyphthalate.

565. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 564 where the oxidatively cleaving agent is:

(1) hydrogen peroxide with a carboxylic acid forming agent.

566. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 565 where the carboxylic acid forming agent is a base.

567. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 566 where the is base is an inorganic base selected from the group consisting of hydroxide,

bicarbonate, and carbonate and organic bases selected from the group consisting of $(Q_3)_3N$ were Q_3 is C_1-C_3 alkyl, DBU, DBN, DABCO, pyridine and *p*-dimethylaminopyridine.

568. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 557 where the base is bicarbonate.

569. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 565 where the carboxylic acid forming agent is an acid .

570. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 569 where the acid is selected from the group consisting of hydrochloric acid, sulfuric acid, phosphoric acid, nitric acid and organic acids of the formula of R_{acid-1}-COOH where R_{acid-1} is –H and C_1-C_3 alkyl optionally substituted with 1 thru 3 –Cl and -F.

571. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 570 where the acid is formic acid and trifluoroacetic acid.

572. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 565 where the carboxylic acid forming agent is an acylating agent.

573. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 572 where the acylating agent is the acylating agent is selected from the group consisting of R_{acid-2}-CO-O-CO-R_{acid-2} where R_{acid-2} is

–H,

C_1-C_3 alkyl optionally substituted with 1 thru 3 –Cl and -F and -φ.

574. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 573 where the acylating agent is acetic anhydride or trifluoracetic anhydride.

575. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 556 where when the reactant is a mixture including a 11α-hydroxy-hydroperoxy compound, the mixture is first treated with a hydroperoxy-deoxygenating agent.

576. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 575 where the hydroperoxy-deoxygenating agent is selected from the group consisting of:

Q_1Q_2S where Q_1 and Q_2 are the same or different and are

C_1-C_4 alkyl,

phenyl,

bisulfite,

sulfite,

thiosulfate,

tetrahydrothiophene,

(C_1-C_4 alkyl)$_3$ phosphite,

(C_1-C_4 alkyl)$_3$ phosphine,

triphenylphosphine,

hydrosulfite,

thiourea,

butyl vinyl ether,

tetramethylethylene.

zinc and acetic acid,

tetramethylethylene and

2-methylfuran.

577. A process to prepare a $\Delta^{9(11)}$-carboxylic acid (VI) according to claim 576 where the hydroperoxy-deoxygenating agent is where Q_1 and Q_2 are both C_1 alkyl and the deoxygenating agent is dimethylsulfide.